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Research Article

Incidence and Determinants of Incipient Diabetic Nephropathy

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Abstract:

Diabetic nephropathy is a late complication of diabetes mellitus. Microalbuminuria is considered to be an early sign of diabetic renal disease. It precedes persistent proteinuria and represents a potentially reversible stage of diabetic nephropathy. This cross-sectional analytical study was carried out on 180 type 2 and 145 type 1 diabetic patients. Patients having clinical albuminuria and with other causes of proteinuria were excluded. Microalbuminuria was observed in 34.48% patients with type 1 diabetes mellitus (DM) and in 28.33% patients with type 2 DM. In logistic regression analysis, high HbA1c, and hypertension were strongly associated with increased albumin excretion in both types of diabetes mellitus. For type 1 DM, other independently associated factors, in order of importance were duration of disease, LDL-C and total cholesterol. Therefore, regular screening for microalbuminuria is recommended for all diabetic patients. Early screening for incipient diabetic nephropathy and aggressive management of these risk factors is important in optimising the renal outcome of patients with diabetes mellitus.

Key Words: Incipient diabetic nephropathy, risk factors, microalbuminuria.

Introduction:

Diabetic nephropathy has long been recognized as a major public health problem with far reaching consequences, not only for its adverse health impact on individuals, but also for its economic burden on the health care system and the society at large.[1] This complication is first manifested as an increase in urinary albumin excretion (microalbuminuria, a stage called incipient nephropathy) which progresses to overt albuminuria and then to renal failure. [2,3] Detection of microalbuminuria is important from a clinical standpoint because, once detected, it is an indication for initiation of appropriate therapy for the purpose of preventing or delaying the advance of progressive diabetic nephropathy. Current recommendations from the American Diabetic association regarding screening for microalbuminuria suggest annual testing after duration of diabetes for 5 years.[4] Recommendations include treatment with angiotensin-converting enzyme (ACE) with persistent elevations in urinary albumin excretion and no other recognized cause of kidney disease. It is important to assess factors related to the development of microalbuminuria in people with diabetes mellitus (DM) in order to identify whether such changes are due to underlying renal pathology or may be related to functional changes. Keeping in view the paucity of data in India, this study was carried out to determine the prevalence of microalbuminuria among Type 1 and Type 2 diabetic patients and to assess the interrelation of microalbuminuria with basic patient socio-demographic features as well as clinical and biochemical parameters.

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Material & Methods:

This study was designed to determine the prevalence of microalbuminuria and the associated risk factors in patients with diabetes mellitus. It was carried out from November, 2009 to September, 2011 after approval of institutional ethical committee. A total of 325 already diagnosed patients of varying age were enrolled for the study; out of which 145 (120 male & 43 females) were of type 1 & 180 (120 males & 60 females) were of type 2 diabetes mellitus. Patients with overt albuminuria, congestive cardiac failure, pre-existing macrovascular condition, urinary tract infection, pregnant females or patients who had given birth within the preceding six weeks and subjects showing disinterest were excluded from the study.

A detailed present and past history of each case was recorded including name, age, sex, address, religion, occupation, economic status, nutritional and personal habits, education, medication and history suggestive of any systemic illness. Weight (Kg) and height (meters) were measured using Omron digital body weight scale and wall mounted metal tapes respectively. Body Mass Index (BMI) was then

calculated for each subject. A BMI less than 25 kg/m^2 was considered as normal, BMI between 25 kg/m^2 and 30 kg/m^2 as overweight and greater than 30kg/m^2 as obesity.[5] All anthropomorphic measures reflect the average of two measurements (measured by the same person on the same instrument to avoid inter-instrument and interpersonal variation). Blood pressure (BP) was measured two times in the sitting position after 10 minutes of rest with a manual mercury sphygmomanometer and the two reading were averaged. Subjects were categoriesed for their blood pressure status according to the Seventh Report of the Joint National Committee (JNC 7).[6] Hypertension stage 2 was defined with a systolic blood pressure equal to or exceeding 160 mmHg or diastolic BP equal to or exceeding 100 mmHg, and those who were in BP lowering medications. Normal blood pressure was considered to be a systolic < 140 mmHg and a diastolic as <90 mmHg. Readings between these levels were classified as stage 1 hypertension. Random urine specimens were collected from all participants at routine medical visits. The urinary albumin concentration was determined by Micral test using commercially available assay kits.[7] The mean inter and intra-assay coefficients of variation were 3.6 and 4.4%, respectively. Normoalbuminuria was defined as Albumin Excretion Rate (AER) < 30 mg/24 hr, and Microalbuminuria as AER 30 to 300 mg/24 hr.[8] Results were confirmed after 2 estimation measurements done in a space of 6 months. If the results of a 2nd estimation placed the patient in a different category from that based on the first estimation, a 3rd urine sample was obtained to confirm either the first or second estimation. After 12 hours of fasting, blood sample was collected for estimation of plasma glucose HbA1c, Serum cholesterol, serum triglycerides and high-density lipoprotein (HDL). Low-density lipoprotein (LDL) cholesterol was calculated with Friedenwald's formula. Adult Treatment Panel III (ATPIII) criteria was used to classify plasma lipid levels.[9] Total cholesterol, triglyceride and LDL levels exceeding 200, 150, and 100 mg/dl respectively, and HDL levels below 45 mg/dl were considered as abnormal.

Data analyses was performed with the SPSS Version 15 statistical software. Two-group comparisons were made using *chi-square* (χ^2) for categorical variables and Student's *t-tests* or one-way ANOVA for continuous variables. For all analyses, the nominal level of statistical significance was<0.05.

Results:

Microalbuminuria was observed in 34.48% [95% confidence interval (CI), 27.6% - 39.2%] in patients with type 1 DM and 28.33%(95% CI, 26.2% - 34.1%) in patients with type 2 DM respectively. The trend was similar when the sexes were examined separately. In both types of diabetes, the prevalence of microalbuminuria rose progressively with increasing levels of fasting plasma glucose, HbA1c and hypertension status (p<0.0001). There was also a progressive increase in the prevalence of microalbuminuria with increasing disease duration in type 1 DM patients only (Table I). However, no relation of microalbuminuria with age, gender, BMI, HDL-C levels, age at onset of DM, mode of treatment, socio-economic status and other lifestyle variations was found.

Table II and III depicts the selected characteristics among the study population with regard to normo albuminuria and microalbuminuria. In type 2 DM all of the variables (except HDL-C) were significantly higher in patients with microalbuminuria compared with patients with normal albumin excretion (Table II). However, for type 1 DM total cholesterol and HDL-C did not differ significantly between patients with normal and elevated albumin excretion (Table III).

Discussion:

This cross sectional study revealed a prevalence of microalbuminuria and its determinants among diabetic patients. The analysis showed an overall prevalence of microalbuminuria of 34.48% among type 1 patients and 28.33% among type 2 diabetic patients. The National Urban Diabetes survey[10] showed the prevalence of diabetes in a population older than 40 years to be 23.8% in 6 cities of India, and the Chennai Urban Rural Epidemiology Study (2003-2004) estimated the prevalence in those older than 40 years to be 30.1%.[11] Several other epidemiological studies reported prevalence rates of microalbuminuria ranging from 7% to 42%.[12-21] The variation in prevalence rates is most probably attributable to differences in design, setting, diagnostic criteria, methods for collection of urine, and its assessment of microalbuminuria and patient population.

In the present study, HbA1c, blood pressure and duration of diabetes (only in type I DM patients) were strongly associated with microalbuminuria, in accordance with other studies.[17,22,25] Significant association was also observed when fasting plasma

Table I: Prevalence of microalbuminuria in diabetic patients with various variables.

	Type 2 DM*				Type 1 DM*			
	n	MAU† n(%)	χ^2	*p*	n	MAU† n(%)	χ^2	*p*
Gender								
Male	120	35(29.16)	0.123	0.726	102	37(36.27)	0.489	0.484
Female	60	16(26.66)			43	13(30.23)		
Age group(years)								
<20	12	1(8.3)			15	2(13.3)		
20-29	40	7(17.5)			39	10(25.6)		
30-39	48	12(25.0)	7.98	0.158	38	13(34.2)	8.45	0.133
40-49	62	20(37.8)			29	13(44.8)		
50-59	10	4(40.0)			15	7(46.6)		
≥60	8	4(50.0)			9	5(55.5)		
B.P.								
Normal	80	12(15)	22.2	<0.0001	59	10(16.9)	15.6	<0.0001
Stage 1 HTN	68	20(29.4)			58	24(41.3)		
Stage 2 HTN	32	19(59.3)			28	16(57.1)		
Glucose-F(mg/dl)				<0.0001				<0.0001
<110	33	4(12.1)	18.4		27	5(18.5)	23.5	
110-150	98	22(22.4)			76	18(23.6)		
>150	49	25(51.0)			42	27(64.2)		
HbA_1C				<0.0001				<0.0001
<8%	107	19(17.7)	15.9		81	15(18.5)	17.5	
8-10%	37	11(29.7)			37	18(48.6)		
>10%	36	21(58.3)			27	17(62.9)		
Duration of DM								<0.0001
<5 years	71	15(21.1)	4.87	0.088	51	7(13.7)	24.8	
5-10 years	67	19(28.4)			59	20(33.9)		
>10 years	42	17(40.5)			35	23(65.8)		
BMI								
<25	133	35(26.3)	1.69	0.430	114	37(32.5)	2.01	0.366
25-30	30	9(30.0)			22	8(36.4)		
>30	17	7(41.2)			9	5(55.5)		
Total Cholesterol(mg/dl)								
≤200	33	5(15.2)	3.46	0.063	58	13(22.4)	6.23	0.013
>200	147	46(31.3)			87	37(42.5)		
Triglyceride(mg/dl)								
≤150	24	3(12.5)	3.42	0.064	22	5(22.8)	1.59	0.208
>150	156	48(30.8)			123	45(36.6)		
LDL-C(mg/dl)								
≤100	41	7(17.0)	3.32	0.069	34	5(14.7)	7.69	0.006
>100	139	44(31.7)			111	45(40.5)		
HDL-C(mg/dl)								
≤45	108	30(27.9)	0.04	0.839	19	6(31.6)	0.08	0.775
>45	72	21(29.2)			126	44(34.9)		

*DM=Diabetes Mellitus, † =Microalbuminuria

glucose concentration was used in place of HbA1c. It is established that once microalbuminuria is present, it is likely to progress to frank proteinuria over the next 5-10 years in 20 to 50% of subjects.[26] Microalbuminuria is also widely acknowledged as an independent risk factor for cardiovascular disease.[27] Similar to other studies[28,29] this study confirms that microalbuminuria is significantly associated with some adverse cardiovascular risk profile. The microalbuminuria positive group had a more deranged lipid profile with higher serum total cholesterol (only in Type 1DM patients), triglycerides, LDL cholesterol levels compared to the microalbuminuria negative group.

Some studies investigated the effect of gender on the incidence of albuminuria.[13,30,31] Varghese et al

Table II: Selected characteristics of type 2 diabetic patients by urinary albumin concentration.

	Total Type 1 Diabetes Mellitus patients (n=145)			
	Normoalbuminuria (n=95)	Microalbuminuria (n=50)	*t*	*p*
Age(years)	39.6±7.3	45.6±6.8	4.8147	<0.0001
Duration of DM (years)	6.4±3.9	10.5±4.4	5.7541	<0.0001
BP-systole(mm/Hg)	126.4±20.2	140.8±18.8	4.1170	<0.0001
BP-diastole(mm/Hg)	82.6±8.2	86.6±7.9	2.8270	0.0054
BMI(kg/m^2)	22.1±3.3	23.6±4.6	2.2617	0.0252
Glucose-F(mg/dl)	134.5±20.6	174.2±24.2	10.3754	<0.0001
HbA1C (%)	7.8±1.6	9.0±1.8	4.1097	<0.0001
Total cholesterol(mg/dl)	212.3±34.7	220.5±30.2	1.4125	0.1600
Triglycerides(mg/dl)	176.7±62.3	210.6±60.1	3.1521	0.0020
HDL-C (mg/dl)	44.8±6.4	43.4±4.1	1.4016	0.1632
LDL-C (mg/dl)	109.2±32.3	146.3±30.4	6.7066	<0.0001

Table III: Selected characteristics of type 1 diabetic patients by urinary albumin concentration.

	Total Type 1 Diabetes Mellitus patients (n=145)			
	Normoalbuminuria (n=95)	Microalbuminuria (n=50)	*t*	*p*
Age(years)	39.6±7.3	45.6±6.8	4.8147	<0.0001
Duration of DM	6.4±3.9	10.5±4.4	5.7541	<0.0001
BP-systole(mm/Hg)	126.4±20.2	140.8±18.8	4.1170	<0.0001
BP-diastole(mm/Hg)	82.6±8.2	86.6±7.9	2.8270	0.0054
BMI(kg/m^2)	22.1±3.3	23.6±4.6	2.2617	0.0252
Glucose-F(mg/dl)	134.5±20.6	174.2±24.2	10.3754	<0.0001
HbA1C (%)	7.8±1.6	9.0±1.8	4.1097	<0.0001
Total cholesterol(mg/dl)	212.3±34.7	220.5±30.2	1.4125	0.1600
Triglycerides(mg/dl)	176.7±62.3	210.6±60.1	3.1521	0.0020
HDL-C (mg/dl)	44.8±6.4	43.4±4.1	1.4016	0.1632
LDL-C (mg/dl)	109.2±32.3	146.3±30.4	6.7066	<0.0001

reported that male sex was independently associated with microalbuminuria.[31] In contrast, an association between sex and microalbuminuria could not be confirmed with the present study, even in univariate analysis. Similarly, no statistically significant relationship of microalbuminuria with age was found in the present study which is in accordance in the other studies. This was at variance with the findings of previous studies.[22,24,31,33]

In the present study, patient with abnormal AER had longer known diabetes duration than those with normal AER 10.5±4.4 versus 6.4±3.9 years (p<0.0001) for type 1 DM and 10.7±4.2 versus 7.5±4.6 years (p<0.0001) for type 2 DM. Similar observation were made by other workers.[13,34,38]

Elevated blood pressure is documented as one of the most significant factor in the pathogenesis and the progression of abnormal AER and eventually development of diabetic nephropathy in both type 1 and type 2 diabetic patients.[17,28,39,41] Hypertension was also one of the major determinants of microalbuminuria in the present study. Univariate analysis revealed significantly higher levels of systolic and diastolic blood pressure in patients with microalbuminuria as compared with patients without microalbuminuria.

Nonetheless, this study has few limitations. Firstly, sampling may not be representative to all patients and/or the general population as undiagnosed subjects may have been excluded. Secondly, the design was cross-sectional and therefore, causal relationship cannot be ascertained. Thirdly, the proxy definition of diabetes mellitus was used in the study and auto antibodies screening such as Anti-GAD analyses was not assessed for patients. As such it is likely that some type 2 diabetes is misclassified as type 1. Other limitations include those inherent to patient reliability or compliance in complete urine collection.

Conclusion:

The prevalence rate of microalbuminuria was considerably high among diabetic patients, and is associated with many potentially modifiable risk factors. Patients and care providers should give the highest priority to improve glycaemic control sufficiently to maintain HbA_{1C} values below 8% along with other modifiable risk factors such as hypertension and lipid levels. If this can be achieved, the number of patients, in whom microalbuminuria develops, should decline. Therefore, regular screening for microalbuminuria is recommended for all diabetic patients. Early screening for incipient diabetic nephropathy and aggressive management of these risk factors is important in optimising the renal outcome of patients with diabetes mellitus.

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Research Article

Efficacy of Intravenous Clonidine & Tramadol on Post Spinal Anaesthesia Shivering in Elective Lower Segment Caesarean Section: A Randomized Comparative Study

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Abstract:

The aim of this study was to evaluate the efficacy, potency and side effects of clonidine as compared to tramadol in post spinal anaesthesia shivering. In this double blind comparative study, 90 American Society Anaesthesiologists grade I & II patients aged between 18-35 years scheduled for elective LSCS under spinal anaesthesia who subsequently developed shivering intra operatively were selected. Equal number of patients were allocated to receive either clonidine 50µg (Gr C) or tramadol 50mg (Gr T). Grade of shivering, disappearance of shivering, haemodynamics and side effects were observed at scheduled intervals. The mean interval between the injection of drug and complete cessation of shivering was significantly earlier in group C than group T. Over all side effects were less in clonidine than tramadol, except sedation. It was concluded that clonidine is more effective in cessation of shivering than tramadol with fewer side effects.

Key Words: Clonidine, Tramadol, Post Spinal Anaesthesia Shivering, Lower Segment Cesarean Section.

Introduction:

Elective lower segment caesarean section (LSCS) is widely performed under spinal anaesthesia. Shivering is known to be a frequent complication, reported in 40 to70% of patients under going surgery under regional anaesthesia.[1,2] Shivering can double or even triple oxygen consumption and carbon di oxide production. Prospective randomized data suggest that high risk patients assigned to only 1.3 degree celsius core hypothermia were three times more likely to experience adverse myocardial outcomes.[3] It also causes arterial hypoxemia, lactic acidosis , increased intraocular pressure, increased intracranial pressure and interferes with pulse rate, blood pressure and electro cardiogram (ECG) monitoring.[4,5,6]

Though the mechanism of origin of shivering is not clear, various hypotheses have been proposed to explain it; pre-operative hypothermia is considered as the primary cause. Various pharmacological and non pharmacological methods have been proposed, of which tramadol[7] & clonidine[8] are the commonly used drugs to control shivering.

This prospective, double blind, randomized clinical study was designed to compare the anti shivering effect & side effects of clonidine and tramadol in the treatment of post spinal shivering in patients under going elective LSCS.

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Material and Methods:

After obtaining permission of the ethical committee of college and written informed consent, 90 ASA I & II patients of age 18 - 35 years, scheduled for elective LSCS, who subsequently developed shivering intra operatively, under spinal anaesthesia, were enrolled by random allocation in this study and divided into two groups of 45 each.

Exclusion criteria included known hypersensitivity to clonidine and tramadol, hyper or hypothyroidism, cardio pulmonary, liver or renal disease, psychological disorder, blood transfusion during surgery, initial body temprature > 38^0C or < 36^0C.

Anaesthetist who were not involved in the study made the trial preparations and recorded group randomization separately. The anaesthetist conducting the case and recording the data were unaware of the preparation administered.

Subarachnoid block was given with inj. Bupivacaine 0.5% (12mg.) at L 3-4 interspace using 25 gauge whiteacre needle and blockage up to T 9-10 dermatome was achieved.

The parturients were randomly (envelop randomization) allocated to receive clonidine 50 µg (Gr C; n = 45) or tramadol 50 mg (Gr T; n=45). Parturients who developed grade 3 or 4 shivering for at least 3 minutes after spinal anaesthesia were included in the

study. Both the drugs were given as slow IV bolus injection. Oxygen was administred to all the patients at a rate of 4 l/min. through venturi mask & patients were covered with drapes but not actively warmed, ambient temprature was maintained at 22-24°C. Intravenous fluids & drugs were administered at room temperature. Preloading was not done in both the groups as we did not want intravenous fluid to influence the onset of shivering mechanism. For the same reason no premedication was given.

Before beginning of spinal anaesthesia, standard monitoring procedure were established. Standard monitoring of pulse rate & oxygen saturation (spO_2) was done continuously and noninvasive blood pressure (NIBP) & axillary body temperature were recorded before the commencement of surgery and there after at every 5 minutes for 1 hours and every 15 minutes for the rest of the observation period.

Grading of shivering was done as follows[9]:

Grade 0: No shivering

Grade 1: One or more of the following: Piloerection, peripheral vasoconstriction, peripheral cyanosis without other cause, but without visible muscle activity.

Grade 2 : Visible muscle activity confined to one muscle group

Grade 3: Visible muscle activity in more than one muscle group

Grade 4: Gross muscle activity involving the whole body

Patients who developed either grade 3 or 4 of shivering were included in the study. The attending anaesthetist recorded the time in minutes at which shivering started after spinal anaesthesia (onset of shivering), severity of the shivering, time of disappearance of shivering (in minutes) and response rate (shivering ceased after treatment in 15 minutes). Duration of surgery was noted and duration of spinal anaesthesia was recorded by assessing spontaneous recovery of sensory block using pin prick method and observing spontaneous movement of limbs in the post operative period. If shivering did not subside by 15 minutes, the treatment was considered to be not effective. Recurrence of shivering was also noticed untill the patients left the operation theatre. Patients who did not respond or in whom recurrence of shivering occurred were treated with additional dose of clonidine (0.5 µg / kg IV) or tramadol (0.5 mg/kg IV) in the respective groups if required. Side effects like nausea, vomiting, bradycardia (<50/Min), Hypotension (> 20 % of baseline), dizziness and sedation score were recorded. Sedation score was assessed with a four point scale as follows:[10]

1. Awake and alert.
2. Drowsy, responsive to verbal stimuli.
3. Drowsy, arousable to physical stimuli.
4. Unarousable.

Bradycardia, hypotension and vomiting were treated with atropine, mephenteramine and metaclopramide, respectively, in titrated doses when required. Statistical analysis was done using suitable statistical software and student t test and chi- square test were applied for the interpretation of results. A p value < 0.05 was considered statistically significant.

Results:

Ninety parturients who experienced shivering of grade 3 and 4 after spinal anaesthesia during caesarean section were included in the study. Parturients characteristic in respect of age, weight, duration of surgery, volume of intravenous fluid administered and duration of spinal block were comparable (Table I).

Shivering disappeared in 43 (95.5%) patients who received clonidine and 41 (91.11%) who received tramadol (Table II).

Severity of shivering was unchanged in 2 (4.5%) patients of group C and 4 (8.8%) patients of group T. Two parturients in group C (severity of shivering unchanged) and 7 parturients (4- severity of shivering unchanged ; 3 recurrence of shivering) in group T were given rescue doses of clonidine or tramadol respectively.

The mean interval between the injection of drug (clonidine and tramadol) and the complete cessation of shivering was 2.59 ± 0.66 minutes in clonidine group & 5.11 ± 0.08 minutes in tramadol group, the difference was statistically significant (p>0.0001). Complication rates were significantly higher in group T than in group C (Table III). Nausea, vomiting & dizziness were higher in group T while more patients of group C were sedated than group T.

Bradycardia occured in 3 patients of group C and 1 patients of group T. In group C, 5 patients suffered from hypotension and 3 patients complained of dry mouth, both of which were not present in group T.

Table I : Demographic data of patients.

Parameter	Group C (n = 45	T(n = 45)
Age (years)	32.81 ± 3.52	31.47 ± 3.63
Wt. (kg)	63 ± 9.6	64 ± 8.9
Duration of surgery (Min.)	58.91 ± 10.15	60 ± 7.20
IV Fluids (ml)	2130.76 ± 200.12	2111.35 ± 207.12
Duration of Spinal Block (Min.)	128.60 ± 9.21	125.87 ± 8

Table II : Post-spinal anaesthesia shivering and responses.

Parameter	Group C (n = 45)	T(n = 45)	*p*-value	Significance
Onset of shivering (Min.)	6.8 ± 3.2	6.4 ± 3.4	0.43	N.S.
Severity of shivering (Grade)	3.1 ± 0.07	3.3 ± 0.04	0.31	N.S.
Time interval from treatment to cessation of shivering (Min.)	2.59 ± 0.66	5.11 ± 0.08	>0.0001	H.S.
Response Rate (%)	43 (95.5%)	41 (91.11%)	-	-
Recurrence of shivering (%)	Nil	3 (6%)	-	-

(N.S. - non significant , H.S. - highly significant)

Table III: Complications in both groups.

Parameter	Group C (n = 45)	T(n = 45)
Nausea	0	30(66.60%)
Vomiting	0	11(24.40%)
Bradycardia	3 (6.66%)	1 (2.22%)
Hypotension	5 (11.11%)	0
Dizziness	0	22 (49.00%)
Dry Mouth	3 (6.66%)	0
Sedation score		
1	30 (66.66)	40 (88.88%)
2	15 (33.33%)	5 (11.11%)

Discussion:

Hypothermia during central neuraxial blockade is common[11] and can be nearly as severe as that observed during general anaesthesia.[12] There are three principal reasons for hypothermia under spinal anaesthesia. First, spinal anaesthesia leads to an internal redistribution of heat from the core to peripheral compartment,[13] secondary to sympathetic block and peripheral vasodilation. Second, loss of thermo-regulatory vasoconstriction below the level of the spinal block leads to increased heat loss from the body surfaces. Third, there is altered thermoregulation under the central neuraxial block, characterized by a decrease in shivering thresholds. In addition rapid administration of cold intravenous fluids contributes to the development of shivering.

Treatment modalities include covering the patient with blankets, application of radiant heat and warming the operating room.[14] The use of warm local anaesthetic solution or warm intravenous fluids has met with various degrees of success.[15] Various pharmacological treatments like IV opioids, alfentanil, pethidine[16] nalbuphine and meperidine[17] opioid analgesic tramadol[18] and 5HT antagonists ondansetron,[19] have been used. Our study was designed to compare efficacy of clonidine, an α2 agonist with that of tramadol, a non opioid analgesic for control of shivering after spinal anesthesia in patients undergoing LSCS.

Clonidine is a centrally acting selective α2 agonist. Clonidine exerts its anti shivering effects at three levels : Hypothalmus, locus coeruleus and spinal cord. At the hypothalamic level, it decreases

thermoregulatory threshold for vasoconstriction and shivering, because hypothalamus has high density of α2 adrenorceptores and hence is effective in treating the established post anaesthetic shivering.[20,21] It also reduces spontaneous firing in locus coeruleus – a pro-shivering centre in pons. At the spinal cord level, it activates the α2 adreno receptors and release of dynorphine, norepinephrine and acetylcholine. The depressor effects of these neurotransmitters at the dorsal horn modulate cutaneous thermal inputs.[22]

Tramadol is an opioid analgesic with opioid action preferably mediated via μ (mu) receptor with minimal effect on kappa and delta binding sites; tramadol also activates the mononergic receptor of the descending neuraxial inhibiting pain pathway. The anti shivering action of tramadol is probably mediated via its opioid or serotonergic and noradrenergic activity or both. [23,24]

In the present study, it was observed that clonidine is as effective as tramadol in treating post spinal shivering, but the time interval from the commencement of treatment to cessation of shivering is quite less with clonidine than with tramadol ($p > 0.0001$).

The response rate was also higher in the clonidine group than in tramadol group but difference was not statistically significant ($p = 0.03$).

In the present study, incidence of nausea, vomiting and dizziness was higher in tramadol group while sedation was higher in clonidine group. Three patients of group T had recurrence of shivering in post operative period, while no patients in clonidine group suffered recurrence.

Bradycardia occurred in 3 patients of group C and 1 patients of group T. While hypotension was more common in group C. On overall analysis, higher complication rate were noted in group T patients compared to group C.

The limitation of this study is that core body temprature was not measured.

Conclusion:

Clonidine 50 μg and tramadol 50mg both are effective in treating post spinal anaesthesia shivering in patients under going LSCS however the side effects were fewer with clonidine. The more frequent incidence of side effects of tramadol may limit its use as an anti shivering drug.

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Research Article

A Morphological Study of Juncturae Tendinae of Hand in Adults and Fetuses

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Abstract:

On the dorsum of the hand, proximal to the metacarpo-phalangeal joints, interconnecting bands called 'juncturae tendinae' extend between the tendons of extensor digitorum longus. These juncturae tendinae are clinically important since the finger extension can be preserved when the extensor digitorum longus is lacerated proximal to the juncturae tendinae connecting that finger to an intact extensor tendon. Varying morphologies of juncturae tendinae have been described in the literature. The knowledge of morphology of juncturae tendinum is important as it has functional and surgical importance. This study was undertaken to observe the morphology of juncturae tendinae in adult cadavers and still born fetuses of South Indian origin. A total of 50 forearms and dorsum of the hands were dissected. This included 30 adult cadaveric hands and 20 still born fetal hands of either sex. The following features of juncturae tendinae were noted: their gross morphology, size, shape and location. Juncturae tendinae were absent in the 1st intermetacarpal space of all the dissected hands. Type 1 juncturae tendinae was present in 68 % of the second intermetacarpal space and in 48% of the third intermetacarpal space. In the 4th intermetacarpal space most of the juncturae tendinae were of '3r' type rather than '3y' type; these types of juncturae tendinae were absent in the second intermetacarpal space as described in the literature. The present anatomical data may help the hand surgeons to modify their surgical procedure for better outcome.

Key Words: Juncturae tendinae, Intertendinous connections

Introduction:

The extensor tendons enter the dorsum of hand through six compartments formed by the extensor retinaculum-a fibrous band that prevents the bow stringing of the tendons. At the wrist the extensor tendons are more round and have sufficient bulk to hold a suture. As the tendons continue into the fingers, they become flat and thin with longitudinal fibers that do not hold sutures well.[1] Despite all tendons involved in finger extension, complete independent extension of each finger is difficult. This is because the mechanism by which the long extensor muscle tendon act is complex. This is in part attributable to the 'juncture tendinum' and 'intertendinous fascia' between the long extensor tendons on the dorsum of the hand. Three different morphological types of juncture tendinum (JT) of the extensor tendons have been described in the literature: *Type 1*- filamentous with inter tendinous fascia, *Type 2*- much thicker and well defined connecting band, *Type 3*- classified into **r** and **y** sub types depending upon the shape[2]. Juncture tendinum are functionally important as they are mainly involved in spacing of extensor digitorum (ED) tendons, force redistribution and stability of metacarpophalangeal joints.[2,3,4,5,6] Juncture tendinum is involved in stabilizing the extensor communis tendons at the metacarpophalangeal joint and also may have a potential destabilizing role, depending on the finger positioning.[7] There are very few studies in the literature describing the morphology of juncturae tendinae, its type and dimensions especially in fetuses. Knowledge of their morphology is of immense importance to surgeons when considering the operative stabilization of unstable extensor tendons. Hence, this study was taken up with the objective to document the morphological types of juncturae tendinae both in adult and fetal cadavers of South Indian origin.

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Material & Methods:

The data for the present study was collected from formalin fixed adult cadavers allotted for undergraduate dissection in the Department of Anatomy, St. John's Medical College, Bangalore and also from a collection of embalmed still born full term fetuses. Extensor compartment of the forearm and the dorsum of the hands were dissected in both the upper extremities of 15 adult cadavers and 10 still born fetuses of either sex. Cadavers with hand anomalies, hematomas, fractures, tumors or lacerations were excluded from the study. A longitudinal incision was made on the back of the forearm and dorsum of the

hand. Three transverse incisions were made, one each at the posterior aspect of elbow, wrist and the base of the proximal phalanges. The extensor muscles and their tendons were exposed in the forearm and the dorsum of hand by reflexion of the skin and the fascia. The extensor tendons to each finger were identified, cleaned and the morphology of the juncturae tendinae were studied using following parameters: gross appearance, size, shape, location and distribution on the dorsum of the hand.[8] The JT were categorized into Types 1 to 3 based on their morphological appearance.[2] The length of the juncturae tendinum was measured as the intertendinous distance along the middle of the JT. The width was measured as the average distance of the juncturae tendinum perpendicular to the length. The location of the JT to the adjacent tendons of origin and insertion in the intermetacarpal (IMC) space were recorded. The first IMC space was defind as the space between the metacarpals of the thumb and index finger, and second, third and fourth spaces as spaces between the index and middle, middle and ring, ring and little finger respectively. Measurements were recorded by means of a digital caliper to the nearest 0.01 mm. All the dissected specimens were photographed with a digital camera.

Results :

Juncturae tendinae was absent in all 1st IMC spaces of adults as well as fetal hands.

In the adult hand, juncturae tendinae was absent in six sides (20%) of the 2nd IMC space; type 1 JT was observed in 22 hands (73.33%); Type 2 JT was found only in two hands (6.66%). Both 3r and 3y types of JT were absent in all the 2nd IMC space (Fig. I; Table I).

In the fetal hand, in 2nd IMC, type 1 JT was present in 12 (60%) hands; types 2 JT was present in only one (5%) hand. Both, type 3r and 3y JT were absent in all the 2nd IMC spaces of fetal hands (Fig. II; Table I).

In 3rd IMC space of adult hands, type 1 JT was found in six (20%) hands; type 2 JT was present in 15 (50%) hands; type 3r JT was present in six (20%) hands and type 3y JT was present in three hands (10%; Fig. I).

In 3rd IMC space of fetal hands, type 1 JT was found in three hand (15%); type 2 JT was observed in nine (45%) hands. Type 3r JT was found in five (25%) and type 3y JT was present in three (15 %) hands (Fig. II).

In 4th IMC space of adult hands, type 1 JT was found in two (6.66%) hands; type 2 JT was observed in six (20%) hands. Type 3r JT was present in 12 hands (40 %) and type 3y JT was present in ten hands (33.33%).

In 4th IMC space of fetal hands, type 1 JT was found in one (5%) hand; type 2 JT was observed in two (10%) hands. Type 3r JT was present in 12 (60%) hands and type 3y JT was present in five (25%) fetal hands.

The dimensions of JT in adults and fetus in each IMC space are shown in the Table II.

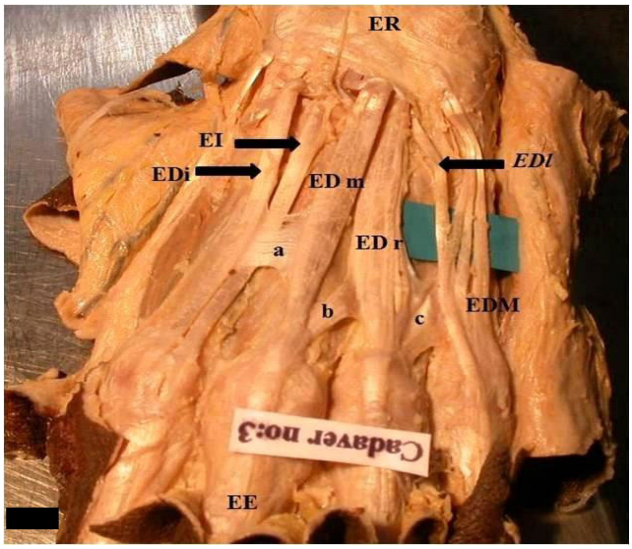

Fig. I: Dorsal view of the adult left hand showing the long extensor tendons.a, b, and c represent the juncturae tendinae (JT) in the second, third and fourth inter- metacarpal spaces (IMCS) respectively. Letter 'a' represents JT type 1 (filamentous type), 'b' is type 2 (thicker and well-defined connecting bands) and 'c' is type 3r.

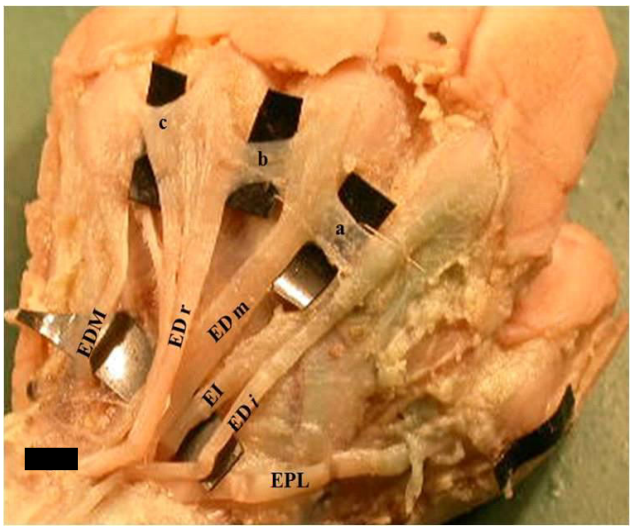

Fig. II: Dorsal view of the left hand of a fetus showing the long extensor tendons and the juncturae tendinae (JT). a, b, c represent the juncture tendinae (JT) in the second, third and fourth inter-metacarpal spaces (IMCS) respectively. a and b represents JT type 1 (filamentous type), and c is type 3y.

Table I: Distribution of Juncturae Tendinae in the Intermetacarpal Spaces of Adult and Fetal Hands.

Type of juncturae	2 ND IMCS			3 RD IMCS			4 TH IMCS		
	Adult	Fetus	Total (%)	Adult	Fetus	Total (%)	Adult	Fetus	Total (%)
TYPE 1	13 R/9 L	4 R/8 L	34(68)	4R/2L	0R/3L	9(18)	1R/1L	1R/0L	3(6)
TYPE 2	1R/1L	1R/0 L	3(6)	8R/7L	5R/4L	24(48)	3R/3L	1R/1L	8(16)
TYPE 3r	0R/0L	0R/0L	0R/0L	3R/3L	2R/3L	11(22)	4R/8L	6R/6L	24(48)
TYPE 3y	0R/0L	0R/0L	0R/0L	0R/3L	1R/2L	6(12)	3R/7L	1R/4L	15(30)
Absent	2 R/4 L	2R/5 L	13(26)	0R/0L	0R/0L	0R/0L	0R/0L	0R/0L	0R/0L

R-Right side; L-Left side; IMCS-Intermetacarpal space.

Table II: Size of JT in Adults and Fetus

TYPE of JT	ADULT		FETUS	
	Length(mm) (Mean±SD)	Width(mm) (Mean±SD)	Length(mm) (Mean±SD)	Width(mm) (Mean±SD)
TYPE 1	9.2± 3.2	11.3 ±2.2	4.73 ±1.2	3.16 ±0.2
TYPE 2	10.1± 1.7	5.1± 1.4	6.1± 1.4	2.3± 1
TYPE 3r	12.3± 1.3	3.8± 1.4	9.6± 1.3	2.1± 0.8
TYPE 3y	15.3± 2.4	3.7± 1.8	8.1 ±1.5	2.1± 0.8

Table III: Comparative Prevalence of Variations in Junture Tendinae

Types of JT		Dass et al, (2011) n=100	Celik et al, (2008) n=54	Von Schroeder, et al, (1990) n=40	Present study (2012) n=30 adult & 20 fetus
*Type1	Between Index & middle finger	83	57.4	88	68
	Between middle and ring finger	9	16.7	28	18
	Between ring and little finger	1	1.8	0	6
*Type 2	Between Index and middle finger	4	3.7	0	6
	Between middle and ring finger	67	59.3	40	48
	Between ring and little finger	15	7.27	20	16
*Type 3r	Between Index and middle finger	0	0	0	0
	Between middle and ring finger	8	14.8	32	22
	Between ring and little finger	73	53.7	80(3r+3y)	48
*Type 3y	Between Index and middle finger	0	0	-	0
	Between middle and ring finger	16	5.5	-	12
	Between ring and little finger	11	37	-	30
*Absent	Between Index and middle finger	13	38.8	12	26
	Between middle and ring finger	0	3.6	0	0
	Between ring and little finger	0	0	0	0

*All figures represent % of incidence;

Discussion:

Juncturae tendinae are oblique intertendinous fiber bands between extensor tendons in the IMC space passing in a distal direction from middle finger to index finger and from ring finger to middle and little fingers. Three distinct morphologic types of JT have been described: Type 1 JT consists of filamentous regions within the intertendinous fascia which is attached to the extensor tendons on either side of the IMC space in a transverse or oblique direction. The type 2 JT consists of much thicker and well-defined connecting bands and type 3 consist of tendon slips from the extensor tendons and are sub-classified into "y" or "r" subtypes depending on its shape.[2] In another study 240 hands were explored and three types of Juncturae tendinae namely: fascia, ligament and tendon were identified.[8] Each hand had three juncturae. The most frequent presentation was for the three juncturae to be fascia-ligament-tendon, from radial to ulnar. Harai et al in a study of 548 upper limbs for intertendinous connections (juncturae tendinae) classified them into type 1 with a filamentous band, type 2 with a fibrous band and type 3 with a tendinous band subdivided into r-shape and y-shape.[9] The most common pattern in their study was type 1 in the second intermetacarpal space (IMCS), type 3r in the third IMCS, and type 3y in the fourth IMCS.

In the present study, the type 1 JT was present most frequently in the second IMC space (68%) followed by the third IMC space (18%) and least in the fourth IMC space (6%). The findings of the present study are comparable with other studies.[10,11] Whereas, von Schroeder et al did not find type 1 JT in the fourth IMC space in his study.[2]

In the present study, highest frequency (48%) of the type 2 JT was found in the 3rd IMC space followed by 16% in the 4th IMC space and the least (6%) in the 2nd IMC space. They are comparable with the other studies. [10,11] von Schroeder et al on the other hand did not find the presence of type 2 JT in the second space in their study.[2]

Type 3 JT can be categorized into r and y types according to the shape. Most of the JT were of 'r' type rather than 'y' type. The r and y types were absent in the second IMC space as described in the literature. The length of the type 3 JT was maximum in adult.

The length and width of the JT in fetal hands was smaller as expected than the adult hands and could not be compared with any other study as there were no reports in the literature related to length and width of JT in fetus. In fetus, type 3 JT was not found in second and third IMC space, type 3y was not found in any of the spaces. Juncturae were absent in all of the first IMC spaces.

The JT between the extensor tendons are of paramount importance in identifying the extensor tendons and to space the extensor tendons, force distribution and stabilization of the metacarpophalangeal joints.[3] The type and direction of JT also explains the interaction between the adjacent fingers which is maximum on ulnar side than radial side due to thick JT on radial side.[2] Morphology of JT is also very important for surgeons in tendinoplasty on dorsum of hand for extensor tendon repair or in reconstruction of the dorsal aponeurosis with JT. Juncturae tendinae reconstruction has been reported as a surgical management for ulnar tendon dislocation after injury without sagittal band damage.[12] The JT also seemed to provide tendon stability after complete sectioning of the small finger radial sagittal band.[13]

A child's hand is not a miniature adult hand. The pediatric musculoskeletal system differs greatly from that of an adult. Although these differences diminish with age, they present unique injury patterns and challenges in the diagnosis and treatment of pediatric orthopedic problems.[14] A child's hand is the most vulnerable body part to get injured. Anatomy of the extensor tendons is extremely important in dealing with the neonatal hand injuries.

Accidental fetal injury is a serious but under reported complication during Caesarean delivery, especially lacerations of the extensor tendons. A number of reports are available in the literature regarding extensor tendon injuries during emergency Caesarean delivery.[15,16,17] These authors have reported an excellent outcome following surgical repair of the lacerated tendons. Miller and Hauge are of the opinion that in contrast to the flexor tendon injuries, extensor tendon repairs have good functional outcome.[18,19]

The present anatomical data may help the hand surgeons operating on new born to modify their surgical procedures for better outcomes.

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Research Article

Hysterectomy – Which Approach?

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Abstract:

Hysterectomy operation is frequently performed on women. In the era of minimal invasive surgery, the route of hysterectomy depends upon numerous clinical variables. The aim of this study was to evaluate & suggest the appropriate approach for hysterectomy.

A total of 250 patients were included in the presents study; they were divided, into three categories: Category I included 50 patients of Pelvic Organ Prolapse (POP) for Vaginal Hysterectomy (VH), Category II included 40 patients who underwent Non Descent Vaginal Hysterectomy (NDVH), Category III included 160 patients who had Total Abdominal Hysterectomy (TAH). Operative time, hemorrhage, wound infection, post- operative analgesia, febrile morbidity, hospital stay and recovery were recorded for each patient.

Indications for hysterectomy were POP, abnormal uterine bleeding (AUB) and fibroid uterus. The study period showed a gradual increase in number of NDVH. Perioperative blood loss, post operative pain score, hospital stay; cost was less in patients with VH/NDVH. Uncomplicated, fast and cost effective technique for removal of uterus remains VH & NDVH.

Non Descent Vaginal Hysterectomy is gaining increased acceptability among patients being minimally invasive with no visible scar.

Key Words: NDVH, TAH, Vaginal Hystrectomy, Microalbuminuria.

Introduction:

Hysterectomy is the commonest major gynaecological surgery performed in women. The first successful Total Abdominal Hysterectomy (TAH) was performed by Charles Clay at Manchester (1843A.D.). Hippocrate (Fifth century B.C.) was the first to refer about Vaginal Hysterectomy (VH) for prolapse and inversion of uterus. Vaginal Hysterectomy was documented by Soreanus of Ephesus (120 A.D.) but Conrad Langenbeck is credited with the first successful V H (1813 A.D.).

Traditionally, the uterus has been removed by abdominal route that gives the opportunity to inspect the ovaries, a major advantage. The vaginal route is being reserved for Pelvic Organ Prolapse (POP). In the 1990's, Laproscopic Assisted Vaginal Hysterectomy (LAVH)[1] developed and gained acceptance. Many Gynecologists opt to develop their skills for the more sophisticated technique of Total Laproscopic Hysterectomy (TLH). Today radical hysterectomy & bilateral pelvic lymphadenectomy is being performed laproscopically[2] and robotic assistance[3] is being used. Single incision TLH, single port of entry i.e. embryonic Natural Orifice Transumbilical Endoscopic Surgery (NOTES)[4] has evolved further. The emphasis on minimally invasive surgery has lead to a resurgence of interest and importance of VH for non-prolapse indications i.e. Non-descent Vaginal Hysterectomy (NDVH) as the scarless hysterectomy.

Ovaries and other abdominal organs may be appraised by non-invasive means such as ultrasonography, computerised tomography, magnetic resonance imaging, positron emission tomography and tumour markers or diagnostic laproscopy. The aim of this study was to evaluate & suggest the appropriate approach for hysterectomy.

Material & Methods:

This study, a retrospective analysis was undertaken in the Department of Obstetrics & Gynecology, NIMS Medical College, Jaipur from January 2009 - July 2011. Patients undergoing emergency or radical hysterectomy were excluded from the study. A total of 250 patients were divided into three categories: Category I (n=50) Patients of Pelvic Organ Prolapse (POP) for Vaginal Hysterectomy (VH), Category II (n =40) Patients who underwent Non Descent Vaginal Hysterectomy (NDVH) and Category III (n =160) Patients who had Total Abdominal Hysterectomy (TAH).

All hysterectomies were done under spinal

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anaesthesia. All abdominal hysterectomies were performed by Richardson's technique[5]. Oophorectomy was done based on age and disease as per patient's informed consent. Non Descent Vaginal Hysterectomy was done by the Ten Step technique[6], two cases where the uterine size was larger than 14 weeks, required morcellation technique to reduce uterine size to facilitate delivery of the uterus. Vaginal Hysterectomy for POP was done by Mayo Ward technique with pelvic floor repair as per associated defects.

All patients received antibiotic prophylaxis: either Ampicillin-Cloxacillin / Ceftriaxone plus Gentamicin or Amikacin plus Metronidazole. The time for surgery was noted from incision to completion. Blood loss was calculated by the anaesthesiologist and surgical team by totaling blood in suction bottle, soakage on mops and blood on drapes. Postoperatively, haemoglobin was estimated on day three. Patients were discharged after fourth postoperative day in the absence of pain and micturitional problems. Hospital stay was calculated from the day of surgery. Postoperative checkups were done weekly at one, two, four, six weeks after discharge. The period of convalescence was counted as number of days after discharge from hospital till full recovery.

Results:

During the study period, 250 Hysterectomies were performed; their breakup is shown in Table I. Category-I accounted for 18.33 to 20.59%; Category-II accounted for only 1.14% cases in 2009, which progressively increased to 17.65% and 35% cases in 2010 & 2011 respectively while Category-III registered a progressive fall from78.41%, in 2009 to 61.76% to 46.67% in 2011.

Table I: Categories of Hysterectomy.

	2009 n= 88	2010 n=102	Jan - Jul 2011 n=60	Total
Category –I	18 (20.45%)	21 (20.59%)	11 (18.33%)	50
Category-II	1 (01.14%)	18 (17.65%)	21 (35.00%)	40
Category-III	69 (78.41%)	63 (61.76%)	28 (46.67%)	160
Total	88	102	60	250

Age wise distribution of the patients is shown in Table – II. The mean age of POP patients who underwent VH and repair in 2009, 2010 & 2011 were 46.4 years, 45.7 years, 47.3 years respectively. Mean ages for patients who underwent NDVH in 2009, 2010 & 2011 was 40 years, 40 years, 42.1 years respectively. Patients who had TAH in 2009, 2010 & 2011 had mean ages of 44.8 years, 45.3 years and 46.1 years.

The indications for hysterectomy for the various catorgreis is shown in Table III.

Analysis was done for measures like operative time, operative blood loss, blood transfusion, postoperative analgesia, postoperative febrile morbidity(temperature > 38^0C), duration of bladder catheterization, development of urinary tract infection, postoperative wound infection and hospital stay. Other factors noted were secondary haemorrhage in the form of bleeding per vaginum, development of vault haematoma, vault granulation and non-healing ulcer over cuff, cuff cellulitis, convalescence period and recovery (Table-IV).

Discussion:

The incidence of vaginal hysterectomy (VH for POP & NDVH) was 21.59% in 2009 which rose to 38.24% and 53.33% in 2010 and 2011 respectively. In the present study VH component for POP has been 18.33% to 20.59%. In Sweden[7] an increase in the rate of VH was recorded from about 4% in 1987 to 31% in 2003. In Finland[8] rate of VH was reported to be 44%, Laproscopic Hysterectomy on 32% and TAH rate of 24%. A Canadian[9] tertiary care facility reported 14% VH and 5.9% LAVH in 2001. In Nigeria[10] rate for VH was 20% between 1994 to 2003. In Saudi Arabia[11], rate for VH was 21% between 1990 and 2002. In the present study rate of VH for POP was similar to the above studies.

Mean age of patients who underwent hysterectomy was 48.5 years in Canada[9] and 45.7 years in Nigeria[10] showing that the majority of patients undergoing hysterectomy are over 45 years of age. The NDVH group being younger due to their motivational counseling for a scar less operation, less surgical pain, early recovery & mobility.

The Canadian[9] study revealed abnormal uterine bleeding (AUB) as the indication for hysterectomy in 37% cases. In Nigeria[10] fibroid uterus was the commonest indication for hysterectomy in 62.3% cases and POP in 13.1% cases. Saudi[11] women underwent hysterectomy for fibroid uterus in 41.6% cases dysfunctional uterine bleeding (DUB) in 27.1%; out of those who underwent VH, 86.5% had POP. In the present study the indications for hysterectomy

Table: II Age wise distribution of the patients.

	2009	2009	2009	2010	2010	2010	2011	2011	2011
	Cat-I	Cat-II	Cat-III	Cat-I	Cat-II	Cat-III	Cat-I	Cat-II	Cat-III
>55 Yrs	4	-	11	3	-	8	2	-	6
45 – 55 Yrs	6	-	28	8	3	26	5	7	10
35 – 45 Yrs	7	1	22	9	9	20	4	9	8
< 35 Yrs	1	-	8	1	6	9	-	5	4
Totals	18	1	69	21	18	63	11	21	28

Table III: Indications for Hysterectomy

	CATEGORY- I	CATEGORY- II	CATEGORY- III
Fibroids	4#	11	37
AUB / DUB	3#	15	43
Adenomyosis	3#	9	25
Prolapse	50	-	3*
Chronic PID^	1#	2	16
Adnexal Mass / Ovarian Tumours	-	1	25
$CIN / Cervical dysplasia	1#	2	6
Endometriosis	-	-	8
Totals	62	40	163

AUB-Abnormal uterine bleeding, DUB-Dysfunctional uterine bleeding . * patients who had large irregular fibroid uterus with anterior vaginal wall prolapse were operated abdominally and triangular piece of vagina with base superiorly was excised and walls were sutured. # 12 patients had Fibroid/AUB/DUB/Adenomyosis/CIN/PID diseases in addition to POP for whom VH with repair surgery was done. $ CIN - Cervical Intraepitheial Neoplasia, ^ PID - Pelvic Inflammatory Disease.

Table IV: Intraoperative & Postoperative parameters

Parameters	Category-I	Category-II	Category-III
Operation time	1hr35min (1hr15min to 2hr30min)	45 min (35mins to 1hr05mins)	1hr20min (1hr05min to 2hr30min)
Intraoperative blood loss	150ml (100-400ml)	60ml (20-150ml)	250ml (80-650ml)
Blood Transfusion	2 patient	Nil	6 patient
Postoperative Analgesia	Required day-1 SOS day-2	Required day-1	Required day-1, day-2 SOS day-3
Postoperative pyrexia	2 patient	1 patient	5 patient
Bladder catheter	48-72hrs	24hrs	48hrs
Development of UTI	2 patient	Nil	2 patient
Wound infection	1 patient	Nil	4 patient
Hospital stay days	7(6-10)	5(4-6)	7(6-10)
Vault haematoma	3 patient	I patient	2 patient
Cuff cellulitis	2 patient	1 patient	2 patient
Vault granulation	2 patient	Nil	1 patient
Convalescence time	3-4 weeks	2-3 weeks	4-6 weeks

was AUB / DUB in 23%, POP in 20%, fibroid uterus in 19.6%, adenomyosis in 14%, adnexal mass / ovarian tumour in 9.8%, chronic PID in 7.2%, cervical dysplasia in 3.4% and endometriosis in 3.0%.

Non descent vaginal hysterectomy took the least operative time, the mean being 45 minutes followed by TAH which on an average took 1 hr 20 mins and VH 1 hr 35 min. Singh & Bansal[12] have reported an average time of 39.07 mins for VH and 45.56 min for TAH. In the present study operative time was longer, due to demonstrative and instructional method necessary for students.

Mean blood loss has been 60ml at NDVH, 150ml during VH and 250ml for TAH in the present study as compared to 35.36gm at VH and 108.5gm at TAH as reported by Singh & Bansal[12]. Two patients in the VH and 6 patients among the TAH group received a blood transfusion.

No case of VH required conversion to abdominal hysterectomy. No ureteric, bladder or intestinal injury occurred in the present study. Londeen et al[13] have reported 1.5% complications for VH, 8 to 9% complications for minimally invasive surgery and 14% complications for abdominal route. In the present study, morbidity was observed in the form of pyrexia in 2% & 3.13% and infections in 2% & 2.5% in the VH and TAH groups respectively. The Finnish[8] study reported 2.6% & 4% complications intraoperatively, while the Saudi[11] study reported 9.6% & 21.6% rates of infection for VH and TAH respectively. The Nigerian report found 30.3% morbidity. Non descent vaginal hysterectomy was associated with the least morbidity.

In the present study Hospital stay has been 5 days in NDVH and 7 days in VH and TAH patients as compared to 3 days for VH and 5.2 days for the TAH patients in the Canadian[9] study while the Singh & Bansal[12] reported 3.71 days for VH and 7.84 days for TAH patients.

Conclusion:

The route of hysterectomy for an individual patient depends on numerous factors such as child birth, POP, uterine size, associated diseases like infection and endometriosis, presence of adnexal mass / ovarian tumours, prior pelvic surgery, suspicion of malignancy, facilities and equipment available and training / skill of the surgeon. The method should be simple, easy, uncomplicated, relatively less time consuming and cost effective for removal of uterus; NDVH has been found to be the suitable mode of surgery, meeting the above criteria.

Worldwide trends are rising towards minimally invasive approach. Natural Orifice Techniques of Surgery such as Vaginal Route remains the primary choice. It is paramount for teaching institutions to meet future clientele requirements. Benefits dictate change; for health care services lower cost. Every training programs must incorporate the NDVH surgical technique, emphasizing as well as imparting efficiently and effectively the operative procedure at all levels of medical education.

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Research Article

Retrospective Study on Clinical Profile of Severe Malaria in Children Admitted in a Tertiary Care Centre of Central India

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Abstract:

Severe malaria is a potentially fatal condition encountered in all age groups and if not treated timely can cause mortality. The present retrospective study was conducted over 4 years (2009-2012) to asses clinical and haemato-biochemical profile of all severe malaria cases admitted in pediatric ICU. Out of 179 cases of malaria, 102 (56.9%) children had severe malaria. Maximum number of patients were of plasmodium falciparum 59 (57.8%), Plasmodium vivax was documented in 13.7% and mixed infection in 27.4% cases. The age of the patients with severe malaria ranged from 4 months to 12 years mean age being 6 year. Sixty four (62.7%) of them were boys and rest of them were girls. Frequent manifestations encountered were severe anemia (65.6%), followed by impaired consciousness (20.5%), hemoglobinuria (19.6%), multiple convulsions (17.6%), circulatory collapse (10.7%), clinical icterus with multisystem involvement (11%), respiratory distress (6.8%), prostration (5.8%), spontaneous bleeding (5.8%), metabolic acidosis (3.9%) and renal impairment (1.9%). Mortality occurred only in children with Plasmodium falciparum infestation. Outcome was favourable in 88.2% children who were discharged after clinical improvement; where as 4.9% patients died and 6.86% critically ill patients left against medical advice.

Key Words: Severe Malaria, Falciparum, Mixed, Vivax.

Introduction:

Malaria in its severe form is one of the leading cause of mortality in all ages in tropical countries. Across the world, South East Asian Region bears the second largest burden of malaria (13.0%), being next only to African region (81.0%). Among South-East Asia region, India shares two-third of the burden (61.0%) followed by Indonesia (22.0%) and Myanmar (12.0%)[1]. Unlike in Africa, where most of the deaths are reported in infants and children, it is seen that in India, the deaths in infants and children below 14 years of age is only 20.6%. According to an estimate, from 2009-2012, Madhya Pradesh, accounted for 6.0% (72 million) of the total population of India (1.23 billion), but contributed to 6.2% of the total cases of malaria[2]. Plasmodium falciparum (Pf) is the main culprit responsible for severe and complicated malaria[3]. Recent studies suggest that Plasmodium vivax (Pv) is also equally responsible for severe form of malaria[4]. According to World Health Organization, severe malaria is defined as a patient with Pf asexual parasitemia plus at least one or more of the following clinical or laboratory features: cerebral malaria, metabolic acidosis, severe anemia, hypoglycemia, hemoglobinura, circulatory collapse, acute renal failure and acute pulmonary edema etc[3]. Most of the research work on profile of severe malaria in children are reported from Africa and few from India[4,5]. But very few published research articles are available from Madhya Pradesh especially from Bhopal district[6]. The aim of the present study, therefore, was to find out clinical and haemato-biochemical profile of severe malaria in children admitted in our setup.

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Material & Methods:

The present study was conducted in Peoples College of Medical Sciences & Research centre, a tertiary care teaching hospital of Bhopal in Central India. Being a teaching hospital and tertiary referral centre, case input is primarily from Bhopal district and also from bordering districts (Vidisha and Raisen district).

This was a retrospective, hospital based clinico-epidemiological study. Case records of confirmed malaria patients admitted between January 2009 to December 2012 were retrieved from medical record department and data was collected in a preformed proforma and analyzed by SPSS 20.0 software. Chi square test was used and $p<0.05$ was

considered significant. Out of 179 children of malaria admitted in the department of paediatric, 102 children satisfied the World Health Organization (WHO) criteria of severe malaria guidelines 2010 and admitted in Pedaiatric Intensive Care Unit[3]. All the criterias of severe malaria were considered except for hyperparasitaemia and hyperlactataemia because these test could not be done in our set up.

Permission from institutional research and ethical committee was taken before commencement of the study.

Results:

In the present study, *P. falciparum* was the main infecting species in both uncomplicated malaria and severe malaria cases (Table I). Maximum number of children got admitted after rainy season and peak admission were from September to November (Fig. I). Year wise distribution of Pf, Pv & mixed infection is shown in Fig. II. Maximum number of patients were of Pf (57.8%); Pv was documented in 13.7% and mixed infection in 27.4% cases.

The age of patients ranged from four months to twelve years with a mean age of 6 years. In the present study, boys (62.7%) outnumbered girls (37.3%). Majority of patients (55.0%) belonged to rural area. Mean duration between appearance of the first symptom and reporting to the department was 8.3 days. Forty percent children had more than one manifestations of severe malaria. Clinical manifestations of these cases remained static over the study period (Table IIa). Prostration was seen more in Pv group while hemoglobinuria was common in Pf group (Table-IIb).

Fever was the chief presenting complaint in almost all the cases (97.0%) and mean temperature at the time of admission was 99.9^0 F (range 98.6^0 F to 104^0 F). Other presenting complaints of children were: repeated vomiting (41.0%), decreased oral acceptance (22.5%), clinical hemoglobinuria (19.6%), cough (18.6%), abdominal pain (16.6%), impaired consciousness (20.5%) and seizures (17.6%).

Of the 21 children with impaired consciousness, eighteen had multiple convulsions. Lumbar puncture was done in 15 of them and CSF was normal. Eleven children had hypotensive shock requiring ionotropic support. Spontaneous bleeding was seen in six patients out of which one patient died and three patients left against medical advice.

All the patients (n=67; 65.6%) with severe anaemia (haemoglobin <5 g/dl) were given packed red blood cell transfusion. Thrombocytopenia was also seen in all the 3 groups 62.7% (Table III). But platelet transfusion was required in only four children (3 were Pf positive and one was of mixed infection). Bilirubin > 3 mg/dl was seen in 13 patients, whereas, clinical jaundice with multisystem involvenment was seen in twelve children. Raised serum transaminases above the normal reference range (SGOT: 30-35 IU/L; SGPT:40-45 IU/L) was seen in (52.9% children, whereas serum transaminases level >150 IU/L was seen in only 10 children. Table III shows that on admission, hyperglycemia was noted in 15 children,

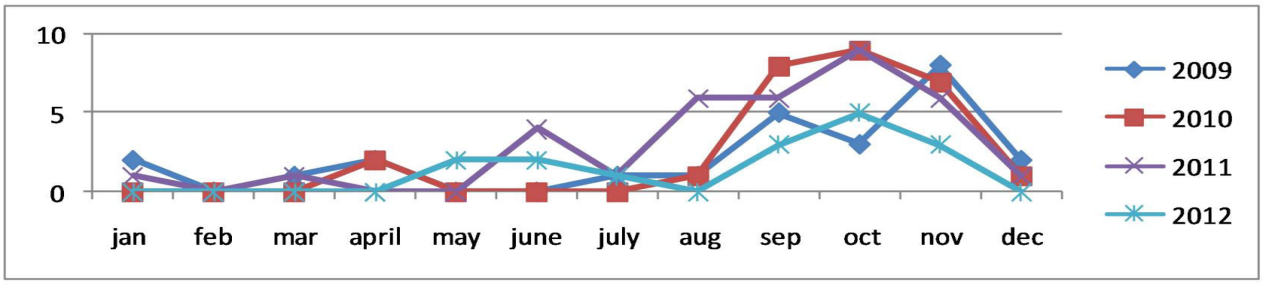

Fig.I: Severe malaria patients admissions during study period.

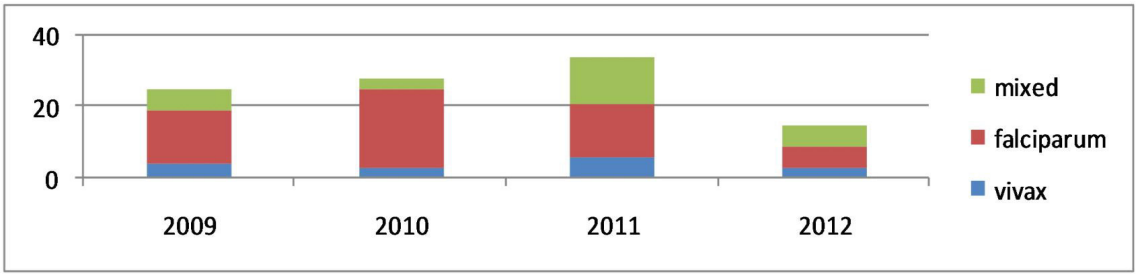

Fig. II: Type of Plasmodium species in severe malaria patients during study period.

Table I: Distribution of admitted malaria cases during study period.

Plasmodium species	Uncomplicated cases	severe malaria	Total
P.falciparum	37 (48.0%)	59(57.8%)	96 (53.6%)
P.vivax	34 (44.1%)	15(13.7%)	49 (27.3%)
Mixed	6 (7.5%)	28 (27.4%)	34 (18.9%)
Total	77 (43.1%)	102 (56.9%)	179 (100%)

Table II (a): Clinical manifestations of severe malaria over four years.

Who criteria	2009 (n=25)	2010 (n=28)	2011 (n=34)	2012 (n=15)	Total
Impaired consciousness	7(28.0%)	5(17.8%)	6(17.64%)	3(20.0%)	21(20.5%)
Prostration	2(8.0%)	1(3.5%%)	2(5.8%)	1(6.6%)	6 (5.8%)
Multiple convulsions	4(16.0%)	6 (21.0%)	7(20.8%)	1(6.6%)	18(17.6%)
Respiratory distress	2(8.0%)	1(3.5%)	3 (8.8%)	1 (6.6%)	7(6.8%)
Circulatory collapse	2(8.0%)	2(7.1%)	5(14.7%)	2(13.3%)	11(10.7%)
Clinical jaundice+MS#	3(12.0%)	3(10.7%)	5(14.7%)	1(6.6%)	12(11.0%)
Spontaneous bleeding	2(8.0%)	1(3.5%)	2(5.8%)	1(6.6%)	6(5.8%)
Normocytic anemia	18(72.0%)	22(78.57%)	17(50.0%)	10(66.6%)	67(65.6%)
Hemoglobinuria	5(20.0%)	4(14.2%)	7(20.5%)	4(26.6%)	20(19.6%)
Renal impairment	0	0	1(2.9%)	1(6.66%)	2(1.9%)
Hypoglycemia	0	0	1(2.9%)	0	1(0.9)
Metabolic acidosis	0	2(7.1%)	1(2.9%)	1(6.66%)	4(3.9%)

Prostration– generalised weakness so that patient cannot walk , , Circulatory collapse – systolic BP < 50 mm hg , # Multisystem involvement i.e. $\geq$ 2 system involvement, Renal impairment- s.creatinine > 265µmol/l, Hypoglycemia- blood glucose < 40 mg/dl , Metabolic acidosis-plasma bicarbonate <15 mmol/l.

Table II (b): Clinical manifestations in Pf, Pv and mixed infection.

Who criteria	P. falciparum (n=59)	P.vivax (n=15)	mixed infection (n=28)	*p*-value
Inpaired consciousness	14(23.0%)	3(20.0%)	4(14.2%)	0.595
Prostration	1(1.6%)	4(26.6%)	1(3.5%)	0.001
Multiple convulsions	11(18.6%)	5(33.0%)	2(7.1%)	0.095
Respiratory distress	5(8.4%)	0	2(7.1%)	0.510
Circulatory collapse	8(13.5%)	0	3(10.7%)	0.319
Clinical jaundice+MS	8 (13.5%)	3(20.0%)	1(3.5%)	0.226
Spontaneous bleeding	3(5.0%)	2(13.3%)	1(3.5%)	0.398
Normocytic anemia	40(67.0%)	7(46.6%)	20 (71.0%)	0.231
Hemoglobinuria	16(27.0%)	0	4 (14.2%)	0.043
Renal impairment	1(1.6%)	1(6.6%)	0	0.315
Hypoglycemia	1(1.6%)	0	0	0.692
Metabolic Acidosis	4(6.7%)	0	0	0.219

three of them required subcutaneous insulin injections. Urinary tract infection was diagnosed in seven patients (pus cells more than 10/mm^3 in uncentrifuged urine) with culture positive of E.coli in one.

Metabolic acidosis was seen in four patients, all of them were P.falciparum positive. Majority of patients with hypoalbuminemia belonged to P.falciparum group. All children of study group were treated with artemisinin combination therapy (ACT) as per WHO guidelines 2010. Outcome was favourable in 88.2% patients who were discharged after clinical recovery; five P.falciparum positive patients died, 2 of them were less than two years of age and both died within few hours of admission in the hospital. Seven very sick patients left against medical advice.

Table III: Associated laboratory abnormalities related to severe malaria

Parameter	n=102	Pf (n=59)	Pv(n=15)	Mixed (n=28)	*p*-value
Thrombocytopenia #	64(62.7%)	39(66.1%)	11(73.3%)	14(50.0%)	0.229
Hypoalbuminemia $	7(6.8%)	6 (10.1)	0	1(3.5%)	0.09
Hyperglycemia*	15(14.7%)	12 (20.3%)	0	3(10.7%)	0.109
Raised bilirubin	13(12.7%)	6 (10.1%)	2 (13.3%)	5(17.8%)	0.061
Increased hepatic enz^	10(9.0%)	7 (11.8%)	3 (20.0%)	0	0.07

Cut off's taken for this study; # Platelet count <1.0 lakh , $ serum albumin <2.5 mg/dl; *Random blood sugar >200 mg/dl, raised bilirubin >3 mg/dl, ^Amonotransferase > 150 IU

Discussion:

This retrospective study revealed that among 102 children with severe malaria, 57.8% patients were positive for P.falciparum. Similar observation were made by Jain et al from Jabalpur[6]. The result of the present study is in contrast to that of Kaushik et al, who reported 24 P.vivax positive patients out of 27 cases of severe malaria[4].

In the present study, maximum number of cases were observed in the months from September to November. However, Tagle & Cabanban reported a maximum number of malaria patients in the month of April from Manila[7].

In a study by Yadav et al[5] cerebral malaria, severe anemia and shock were more frequently observed in P.falciparum group, while hepatic, renal, respiratory, and bleeding complications were more commonly seen in P.vivax positive patients. In the present study, there was no statistically significant difference in clinical manifestations among all the three groups except for the prostration which was more frequent in P.vivax group and hemoglobinuria in P.falciparum group.

In 84.0% of patients, fever responded to first dose of Artesunate. This is in accordance with the results reported by Arnaud[8]. Fever was followed by impaired consciousness in 21 patients, 4 of them had unarousable coma and 2 died within few hours of admission.

In the present study, 67(65.6%) patients had severe anaemia out of which 2 died and 4 critically ill patients left against medical advice. Arnaud et al[8] also reported that severe anaemia (67.8%,) was the commonest feature of severe malaria. The pathophysiology of anaemia in malaria is multifactorial.It results from accelerated red cell destruction and removal by the spleen in conjunction with ineffective erythropoiesis.

Thrombocytopenia is considered to be caused by increased splenic sequestration , immune mediated destruction and shortened platelet survival. In the present study, thrombocytopenia was seen in 62.7% patients. Though thrombocytopenia was more (73.0%) common in vivax group but profound fall (<20,000 platelet count) was seen in P.falciparum group, 3 of them required platelet transfusion. The result is similar to that reported by Shelthy et al from Karnataka[9]. Leukocytosis was seen in 14.7% and leucopenia in 7.8% patients in the present study. Both leucocytosis and leucopenia are known in malaria although there is paucity of literature in pediatric age group[10,11].

High coloured urine (clinical hemoglobinuria) was present in 20 patients on admission which got cleared in few days. Routine microscopy of urine did not show RBCs in any of the patient. Only one patient was found to be G-6PD deficient in our study. The results are consistent with those of Wasiu et al[12].

Jaundice in malaria results from hemolysis of both parasitized and non-parasitized red cells as well as malarial hepatitis. Raised liver enzymes occurs because of injury to hepatocyte and cholestasis. In the present study, a total bilirubin of more than 3 mg/dl was seen in 12.7% children whereas, clinical jaundice with multisystem involvement was seen in 11.0% children. Hepatitis was present in 9.0% of children as indicated by elevated levels of enzymes although other causes of hepatitis were not ruled out. There is scarcity of published literature on malarial hepatopathy in children. In acute malaria, hepatic dysfunction is reversible and patients respond favourably to antimalarial therapy with no residual effects[13].

The sequestration of erythrocytes, containing metabolically active parasite in the vascular bed of internal organs can elucidate almost all the pathological events in severe and complicated P.falciparum malaria. Malarial parasites also induces the release of cytokines like TNF-alpha, IL-1 and IL-6 that initiate many of the pathological process causing manifestations of malaria.

Atypical presentation encountered in the present study was hyperglycemia which was found in 14.0% children; it could be explained as stress induced

hyperglycemia.Stress induced hyperglycemia commonly occurs during critical illness in children, even in those with previously normal glucose homeostasis[14]. Hyperglycemia in severe malaria was also reported by Dass et al[15]. Acute Disseminated Encephalomyelitis (ADEM) was seen in one patient who was P.vwax positive and diagnosed by MRI; it was also reported by Goyal et al[16].

A total of 5 patients died; all of them were P.falciparum positive and had more than one manifestations of severe malaria. It was also reported by Tripathy et al[17]. Three of them died within the first 24 hours of hospitalization. This is in accordance with the result reported by from Kenya by Obonyo et al[18].

Since this was a retrospective study with small sample size, we could not demonstrate any cyclical changes in clinical profile of severe malaria over a period of four years. There is a need of prospective study with bigger sample size to find out any changing trend over years.

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Research Article

Correlation of Admission Test with Neonatal Outcome

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Abstract:

Cardiotocography recordings of both high risk and low risk pregnant women were studied and the results were correlated with the labour outcome, perinatal mortality and various morbidity variables such as 5 min apgar score and intrapartum fetal distress. The results were statistically analysed and the diagnostic value of admission test in terms of sensitivity and specificity in predicting the labour and perinatal outcome has been calculated. Although the majority of the patients in all the trace pattern groups showed Apgar score of >7 but still a clear trend was seen as the number of neonates with apgar score of >7 decreases and the number of neonates with apgar score of <7 increases as the admission test changes from normal to pathological.

Key Words: CTG, foetal distress, Apgar score.

Introduction:

The intrapartum assessment of fetal well being has become an integral part of the management of labour. The cardiotocography (CTG) has a major role to play in such situations because it is simple, easy to perform, non-invasive, inexpensive and has no contraindications.

Cardiotocography is a test that graphically records the fetal heart activity and uterine contractions, simultaneously and continuously, in the same time scale , with fetal movements. The fetal heart rate is obtained via an ultrasound transducer attached to the maternal abdomen. A tocotransducer can also be attached to the maternal abdomen to detect the uterine activity. Both transducers are connected to a cardiotocography machine which produces a two – channel recording on thermal paper, available for interpretation and storage. It is generally agreed that the CTG has a predictive value for fetal outcome and several studies have shown a low false negative rate.

The Admission test , first described by Ingemarsson et al[1] is a short strip (20 minute) of CTG done during labour. It is a dynamic screening test for the state of oxygenation of the fetus on admission of the mother into labour room. It assesses the placental reserve by checking the response of the fetal heart during the phase of temporary occlusion of the utero-placental blood supply under physiological stress of repeated uterine contractions. It thereby assesses the ability of the fetus to withstand the process of labour. Therefore, based on the assumption that early uterine contractions may serve as a functional stress to the fetus, an admission test might detect fetal intrauterine hypoxia present already at admission and might have some predictive value of asphyxia that might develop in early labour.

The Admission CTG thus has two potential roles. It can be used as a screening test in early labour to detect compromised fetuses on admission and to select the women in need of continuous fetal electronic monitoring during labour[2].

The normal fetal heart rate (FHR) at term is 110-160 beats per minute (bpm)[3]. It exhibits periodic variations resulting from autonomic influences. A normal pattern includes baseline variability of 5-25 bpm and at least 2 accelerations in a 20 minute period. An acceleration is an increase in FHR from the baseline by 15bpm for 15 seconds or more[3]. A normal pattern reflects a metabolically and functionally intact fetal central nervous system.

A deceleration is a reduction in the FHR by 15 bpm from the baseline for 15 seconds or more. Decelerations indicate episodes of fetal stress. Early decelerations coincide with the duration of uterine contractions and are common in late first stage and second stage of labour when the fetal head is compressed during its descent through the pelvis. Late decelerations last beyond the duration of a contraction and reflect a reduction of blood flow into the uteroplacental pool, causing transient fetal hypoxia. Variable decelerations reflect fetal umbilical cord compression.

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The National Institute of Clinical Excellence (NICE) and the Royal College of Obstetricians and Gynaecologists (RCOG) have categorised the FHR features and traces as normal, suspicious and pathological[3].

The clinical effectiveness of CTG is reduced by variable and inconsistent interpretation , even among experts, leading to inappropriate interventions for benign patterns and delayed or no intervention for abnormal patterns. There is, therefore, a need for continuing education on CTG interpretation to improve its value in clinical practice. However the advantages of the admission test (non invasiveness, short duration , patient acceptance) have overridden the concerns about its lack of specificity. Abnormal CTG with fetal scalp pH study is more specific of fetal distress and hypoxia than CTG alone.

Material & Methods:

This is a prospective observational clinical study conducted in a tertiary care hospital of Subharti Medical College, Meerut, over a period of 12 months with a sample size of 500 patient.

a). Inclusion Criteria: Pregnancies >32 weeks and <41 weeks of gestation irrespective of the parity.

b). Exclusion Criteria: Pregnancies <32 weeks of gestation, pregnancies with known congenital anomalies, multiple pregnancies, malpresentations, use of sedative in mother before testing, patients with false labour pains, patients with an admission to delivery interval more than 24 hours and patients undergoing elective caesarean section.

The patients admitted to the labour ward were confirmed to be in labour. All patients admitted for induction had cervical priming with intracervical prostaglandin E_2 gel. The admission test for these patients was done once they started having uterine contractions.

A preliminary history was taken and a general and obstetric examination done. The patients will then be subjected to a 20 min CTG recording (paper speed 1cm/min) on a corometrics 170 series machine. The results of the admission test were categorised into normal, suspicious or pathological groups as per the RCOG guidelines[4] for the interpretation of CTG tracings.

Patients with a normal admission test were monitored by intermittent auscultation for one minute, every 30 min in the first stage of labour and every 5 min in the second stage of labour. Those having suspicious or pathological FHR tracings were placed on continuous CTG monitoring. The patients were then followed up for the mode of delivery and the different variables of perinatal outcome collected at the time of delivery.

Table I: Categorisation of fetal heart rate traces [3]:

Category	Definition
Normal	A cardiotocograph where all four features fall into the reassuring category
Suspicious	A cardiotocograph whose features fall into one of the non-reassuring categories and the remainder of the features are reassuring
Pathological	A cardiotocograph whose features fall into two or more non-reassuring categories or one or more abnormal categories

All the patients delivered within 24 hours of the admission test. A fetus/neonate was considered to have distress if any of the following were present: – a) Meconium staining of liquor in labour, b) FHR variations in labour, c) Apgar score of less than 7 at 1 and 5 min. and d) need for intensive neonatal care in specialist nursery. In the case of NICU admission, the neonate was followed up for a duration of 7 days after birth for perinatal mortality and morbidity.

Observations

The maximum number maximum number (276) of patients belonged to 26 – 30 years age group, followed by 122 in 31 – 35 years age group and 83 in 21-25 years age group. There were only 11 patients in > 35 years age group and 8 patients were < 20 years of age. Three hundred seventy one patients were of 37 – 40 weeks gestation and 110 were of 32 – 37 weeks gestation. There were only 19 patients in the 40-41 weeks gestational period. The study population comprised of 268 primigravida and 232 multigravida.

Of the total 500 cases, 130 were high risk and 370 were low risk pregnancies; 275 were admitted with spontaneous labour pains, 129 for induction of labour and 96 with premature rupture of membranes.

Table III shows that as per CTG , 401 patient showed normal pattern, 62 showed a suspicious traces and 37 had a pathological traces.

In the present study, fetal distress was seen in 139 patients. Only 64 (16.0%) cases developed fetal distress in the normal admission test group whereas, the percentage increased to 39 (62.9%) and 36 (97.3%) in the suspicious and pathological group respectively. Out of these 59 neonates had NICU admission. The

Table II: Categorisation of fetal heart rate (FHR) features:

Feature	Baseline (bpm)*	Variability (bpm)*	Decelerations	Accelerations
Reassuring (Normal)	110–160	≥ 5	None	Present
Non-reassuring	100–109 161–180	<5to>40 for <90 minutes	Early deceleration/variable deceleration Single prolonged deceleration upto 3 minutes	The absence of accelerations with an otherwise normal CTG is of uncertain significance
Abnormal (Pathological)	<100 or >180 Sinusoidal pattern >10 minutes	<5 for >90 minutes	Atypical variable decelerations Late decelerations single prolonged deceleration >3 minutes	

(*bpm-beats per minute)

Table III: Results of Labour admission test.

Labour admission test	Number (n=500)	Percentage	95%CI
Normal	401	80.2	76.48-83.46
Suspicious	62	12.4	9.79-16.58
Pathological	37	7.4	5.42-10.03

Table IV: Association of Admission test and Apgar score.

Admission test	Number of cases	Apgar score	
		>7	< 7.0
Normal	401	390(97.3%)	11(2.7%)
Suspicious	62	57(91.9%)	5(8.1%)
Pathological	37	25(67.6%)	12(32.4%)
Total	500	472(94.4%)	28(5.6%)
Inference	Suspicious and Pathological admission test is significantly associated with Low apgar score with $p<0.001$		

different variables of perinatal outcome were collected at the time of delivery. Fifty seven neonates developed fetal heart variation during labour, 54 showed presence of meconium stained liquor and 28 neonates had low apgar score (less than 7 at 1 and 5 min).

Among the patients with a normal admission test, the neonates with low apgar score were quite few (2.7%). With a suspicious admission test, 8.1% neonates had low apgar score while with a pathological admission test, 32.4% neonates had low apgar score.

Although the majority of the patients in all the trace pattern groups showed Apgar score of >7 but it was clear that as the admission test changes from normal to pathological, the number of neonates with apgar score of < 7 increased. Thus, the inference is that the suspicious and pathological admission test is significantly associated with low apgar score ($p<0.001$).

Discussion:

Das et al[5] conducted a prospective randomised study to prove the efficacy of admission test in predicting fetal jeopardy during labour. They reported that incidence of fetal distress and chances of caesarean delivery were higher in the abnormal admission test group. The number of asphyxiated neonates, neonatal admissions, neonatal mortality and the passage of meconium was also higher in the abnormal admission test group. Hegde et al[6] in their study on 200 low risk patients found that as the admission test became suspicious or ominous, fetal distress increased and the incidence of operative delivery also increased. Kushtagi et al[7] conducted a similar study on 500 patients and concluded that labour admission test is of some predictive value , at least for the first few hours after admission in labour.

Sandhu et al[8] conducted a prospective study to predict the neonatal outcome in high risk obstetric cases by admission cardiotocography testing. The results showed that admission CTG could be used to identify patients likely to develop adverse fetal outcomes and help in optimal utilization of labour room resources.

Ingemarsson et al[1] carried out a study in over 1000 low risk women and observed that 40% of patients with ominous admission test developed fetal distress as compared to 1.4% with reactive admission test.

Patients included in the present study were from high risk as well as low risk group. There were 401 patients (80.2%) having normal admission test and 62 patients (12.4%) showing suspicious and 37 patients (7.4%) with pathological pattern (Table IV).

Table V: Comparison of studies for admission test outcome.

Study	Senstivity (%)	Specificity (%)	PPV (%)	NPV (%)
Das et al[5]	38	79	48	72
Hegde et al[6]	66.7	90	38.7	96
Ingemarsson et al[1]	23.5	99.4	40	98.7
Kushtagi et al[7]	53	93	61	91
Sandhu et al[8]	42.3	95.6	73.3	84
Present study	53.96	93.35	75.76	84.04

PPV-Positive predictive value; NPV-Negative predictive value

Table VI: Comparative incidence of fetal distress in relation to admission test in various studies.

Study	Hegde et al[6] (n=200)			Sandhu et al[8] (n=150)			Present study (n=500)		
LAT	R	S	O	N	S	P	N	S	P
No.	169	19	12	101	34	15	401	62	37
FD No.	6	3	9	15	19	11	64	39	36
Fd %	3.6	15	75	15	55	73	16	62.9	97.3

(LAT- Labour admission test; R- Reactive; S- Suspicious; O-Ominous; N-Normal; P-Pathological; FD-Fetal Distress)

In the present study, the sensitivity and specificity are comparable to that of Kushtagi et al[7], Sandhu et al[8] and Hegde et al[6]. The positive predictive value and negative predictive value is comparable to Sandhu et al[8]. The values of the above comparison shows that admission test can be used with great reliability to detect fetuses who are hypoxic and need continuous monitoring and immediate intervention.

Hegde et al[6] observed that the number of cases with fetal distress increased as the admission test changed from reactive to ominous pattern. Sandhu et al[8] also reported a significant rise in the number of cases with fetal distress if the admission test was suspicious or pathological. The present study, showed similar trend. Therefore, it is evident from all the studies that the incidence of fetal distress increases as the traces become suspicious or pathological.

Das et al[5] observed that there was a marked difference in the number of asphyxiated neonates (Apgar score <7 at 5 min.) in abnormal admission test group (8.7%) versus reactive admission test group (1.6%). Neonatal admissions were 3.93 times higher with abnormal admission test and neonatal mortality was also higher with abnormal admission test as compared to reactive admission test group irrespective of high or low risk factors. Presence of fresh meconium in amniotic fluid showed greater correlation with abnormal admission test. Kushtagi et al[7] observed that when the labour admission test was reactive, irrespective of the antenatal risk status, 91.7% did not develop fetal distress. Though 8.3% cases showed fetal distress in spite of reactive admission test, the incidence of fetal distress with suspicious/ ominous patterns were significantly higher. Similar results were observed in the present study and it was seen that more fetal distress cases occurred in the high risk group than the low risk group and the labour admission test served as a useful tool in defining the current risk status in both these groups.

Conclusion:

It is evident from the results of the present study that admission test can be used as an important non-invasive method to diagnose fetal compromise present at the time of admission in high as well as low risk patients in early labour. The advantages of the admission test is that it is non invasive, of short duration and well accepted by patients. The admission test cannot be expected to predict the development of any acute asphyxial insult during the course of labour. In the absence of such acute events, an adverse fetal outcome is unlikely if the admission test is normal. The result of admission CTG testing can be used to identify patients likely to develop adverse fetal outcome and help in optimal utilization of limited labour room resources. This is particularly relevant in situations where the antenatal attendance and follow up has been inadequate. Abnormal CTG with fetal scalp pH study is more specific of fetal distress and hypoxia than CTG alone.

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Case Report

Right Paraduodenal Hernia - A Case Report

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Abstract:

Internal hernias are rare congenital malformation. They present with nonspecific complaints and are therefore, often under diagnosed. Right Paraduodenal hernia accounts for 25% of Paraduodenal hernias. Radiological examination plays a very important role in the diagnosis.

Key Words: Paraduodenal Hernia, Internal Hernia.

Introduction:

Internal hernias are important but under diagnosed entities. The clinical symptoms are non specific & usually include nausea and intermittent pain. Therefore, imaging studies play an important role in the diagnosis and timely management.

The most common internal hernias are paraduodenal hernias (53 %) followed by peri caecal hernias (13 %). Paraduodenal hernia is a rare congenital malformation caused by congenital intestinal protrusion and malrotation through normal or abnormal opening in the mesentery of the colon related to embryologic rotation of the mid gut and variation in the peritoneal fixation & folds[1].

We have recently observed a patient with right Paraduodenal hernia diagnosed preoperatively. It is emphasized that internal hernias should be considered as a diagnosis whenever atypical abdominal symptoms are present.

Case Report:

A-32 year old male patient came with pain and distention of abdomen off and on for which he took symptomatic treatment and was relived from time to time.

On physical examination, his general condition was found to be stable with pulse rate of 82 per minute, Blood pressure 110/80mm of Hg. His systemic examination was within normal limit.

The plain X-ray study of abdomen revealed dilated small bowel loops clustered in right hypochondrium (Fig. I).

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Fig. I: Plain X-ray of abdomen showing dilated small bowel loops (arrows) clustered in right hypochondrial region.

Upper GI Barium study revealed spherical encapsulation of Barium filled jejunal loops to the right side of abdomen. Stomach & duodenum appeared normal (Fig. II).

The CECT study demonstrated encapsulated loops of small bowel in the right mid abdomen. The superior mesenteric vein was rotated anteriorly and to the left of it's normal position and there was looping of arterial and venous jejunal branches behind the superior mesenteric artery into the hernial sac (Fig. III).

On laprotomy right sided internally herniated jejunal bowel loop were seen (Fig. IV).

Discussion:

Abdominal hernias can be subdivided in to two types, internal and external. Internal hernias remain within the abdominal cavity, while external hernias protrude through the defects in abdominal wall. The majority of internal hernias result from a congenital anomalies of intestinal rotation and peritoneal attachment. They are named after the location of the orifices through which they protrude. The most common internal hernias are

Fig.II: Conventional barium meal study revealed spherical encapsulation of jejunal loops to the right side of abdomen (arrow)

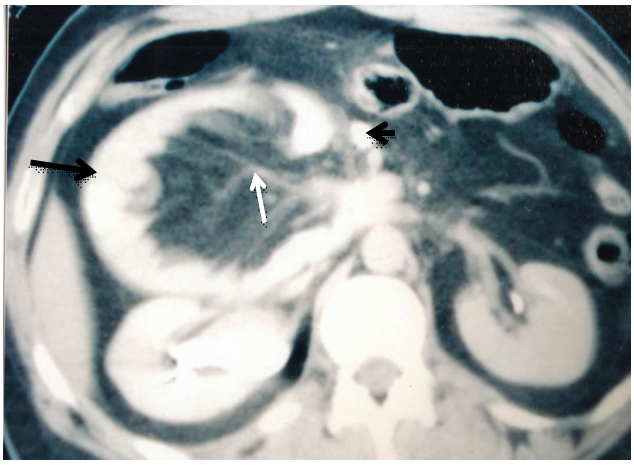

Fig. III: CECT scan of abdomen showing stretched and encapsulated contrast filled small bowel loops in the right side of abdomen (black arrow). The superior mesentric vein is rotated anteriorly and to the left of its normal position (black arrow head). There is looping of arterial and venous jejunal branches behind the superior mesentric artery into the hernial sac (white arrow).

Paraduodenal hernia followed by peri-caecal hernias.

In 1923, however, Andrews declared the term paraduodenal hernia's, a misnomer. According to him, and generally accepted today, paraduodenal hernia is due to incomplete rotation of the midgut and is congenital in origin.

When the fetus is 6 weeks old the midgut herniates into the umbilical cord. It then rotates 90° while in the umbilical cord, 90° on its way back into the abdomen, and a final 90° within the abdomen to rotate a full 270° counterclockwise around the superior mesenteric artery. If the pre-arterial segment rotates

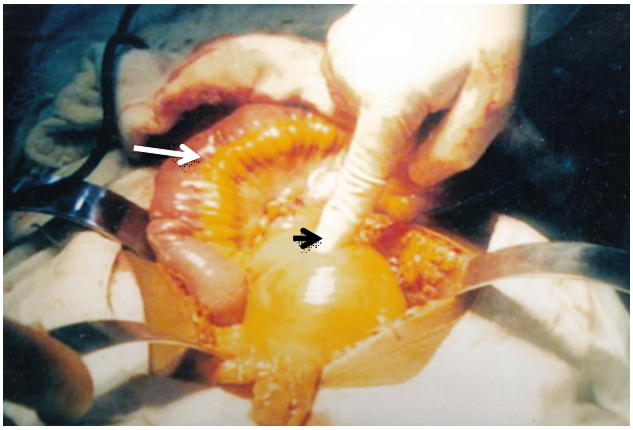

Fig. IV: Operative picture showing rotated small bowel loop (white arrow) in hernial sac (arrow head).

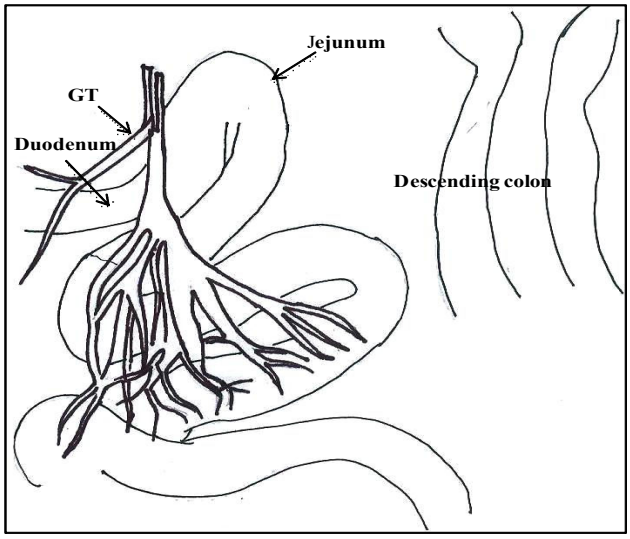

Fig.V: Line diagram showing a right paraduodenal hernia into the fossa of Waldeyer behind the branches of the superior mesenteric artery and vein.

but the post arterial segment fails to rotate the small bowel is entrapped in the right mesocolon, and right Paraduodenal hernia results[2].

Paraduodenal hernias are the most common types. They are basically congenital in origin representing entrapment of the small intestine beneath the mesentery of the colon related to embryological rotation of the mid gut and variation in peritoneal fixation and vascular folds. 75% of Paraduodenal hernias occur on left side and 25% on right side.

The right Paraduodenal fossa of Waldeyer is present in 1% of autopsy cases. It is situated within the first part of mesentery of jejunum, immediately behind the superior mesentery artery and inferior to transverse duodenum. It is bounded posteriorly by abdominal wall (Fig. V)[3-5].

Right Paraduodenal hernias protrude into the ascending mesocolon involving the fossa of Waldeyer

immediately behind the superior mesenteric artery and inferior to third portion of duodenum. The clinical manifestation may range from intermittent mid digestive complaints to acute intestinal obstruction and strangulation. The history of chronic indigestion or periodic nonspecific complaints of parandial pain is a characteristic symptoms and may be relieved by postural changes.

The preoperative diagnosis of Paraduodenal hernia can be established only by Radiological examination especially when the study is performed during symptomatic period in view of the intermittent nature of herniation. Small right Paraduodenal hernias, present as ovoid grouping of small bowel loops lateral and inferior to the descending duodenum. The encapsulation within the hernial sac prevents separation and displacement of individual loops from the rest of the hernial contents during fluoroscopic manipulation. Both the afferent and efferent loops appear closely apposed and narrow in a right Paraduodenal hernia[6]. Not only the intestinal loops, but both the mesentery and vessels are also incorporated into hernia. In a right Paraduodenal hernia the jejunal arteries that normally arise from the left side, reverse their direction and course behind the parent vessels to supply the herniated jejunal loops within the fossa of Waldeyer[7].

The major CT findings are looping of jejunal branches of superior mesenteric artery and vein to the right and posterior and clustering of small bowel loops in right mid abdomen.

Conclusion:

Paraduodenal hernia remains an elusive diagnosis. A solid understanding of the Paraduodenal folds & fossa and the embryological development, therefore, is important to make the diagnosis. It is important for both radiologist and surgeons to be well aware of this condition, especially in the patient with chronic recurrent abdominal pain.

The internal hernia should always be held in due consideration at the moment of diagnosis because the consequent mortality due to complications such as intestinal gangrene is high.

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Case Report

Os Inca Totum-Anthropological and Embryological Basis

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Abstract:

Complete division of membranous and cartilaginous part of occipital bone by a transverse suture extending between the two lambdoid sutures at the level of highest nuchal line above the external occipital protuberance, results in a rare cranial variation presenting as Os Inca totum.

During oesteological study of human skull in the central India region, one male skull showing complete undivided Inca bone was found. The interparital bone is formed by the part of the squamous occipital bone that is bounded by two lambdoid sutures on two sides and inferiorly by transverse suture. Such finding is rare in occurrence and have a significant anthropological and embryological basis.

Key Words: Inca bone, highest nuchal line, lambdoid suture, transverse suture.

Introduction:

The interparital part of occipital bone may be divided by a transverse suture at the level of highest nuchal line. Squamous part of occipital bone above this suture is the Inca bone described by various authors. It was first described by Rivero & Tschudy (1851) in cranium of Peruvian origin[1]. The same variation was also described as Os interparitale.[2]

Transverse suture extends between the two lambdoid sutures at the highest nuchal line above the external occipital protuberance dividing the membranous and cartilaginous part of occipital bone. The Inca bone may be subdivided by the presence of additional longitudinal and transverse suture leading to bipartite, tripartite and multipartite Inca bones.[3]

The frequency distribution of the Inca bone in modern populations has been reported by various observers in different populations. The incidence of the complete Inca bone is very low in the western hemisphere of the old world i.e. Europe and Asia except for sub-Saharan Africa. Among the modern population originally derived from eastern Asian population, the frequencies are highest in some of the marginal isolated groups. In Indian sub-continental population, relatively low incidence of complete Inca bone has been reported. [4,-10]

Observation:

Occipital bone forming the back and base of the cranium, is trapezoid in shaps and internally concave. It encloses the foramen magnum, expanded plate posterosuperior to this is squama, and the massive quadrilateral part anterior to foramen magnum is basilar part. On each side of the foramen is lateral part. Squama is convex externally with external occipital protuberance along with two curved lines extending laterally called as superior nuchal lines and above it to faintly perceptible highest nuchal line. The superior angle at the squama summit meets the occipital angle of parital bones. The lateral angles of the squama project between the parital and temporal bones. The lambdoid borders extend from superior to lateral angles. Variety of ossicles may occur at or near the lambda known as inter-parital ossicles.[11]

During the oesteological study of 270 human skulls in central India region, we found one case of Os Inca Totum. One male skull showed presence of transverse suture measuring 115mm between two lambdoid sutures that subdivided the occipital bone into two parts resulting in formation of os Inca totum. Measurements of Inca bone was 85mm X 115mm X 80mm. It belonged to type III classification of Hanihara & Ishida (Fig. I).[12] The presence of os Inca totum is associated with the two sutural bones in the region of squamous interparital bone at the lambdoid suture.

Discussion:

Anthropologically, the occurrence of Os Inca totum in fossils of hominids such as Australopithecus, Homo erectus and early homosapiens was described by various authors. [9,13] Presence of Inca bone was important primitive feature found in Chinese Homo

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erectus and early Homo sapiens also.[14] Thus the Inca bone is regarded as one of the character that forms the morphological basis of multiregional model of origin of modern human population in east Asian region.[15] Pedigree studies showed that the Inca bone is inherited as dominant trait with 50% penetrance and suggested a genetic background for occurrence of Inca bone.[16]

Cranial deformation in order to achieve distinctive characteristics for special group affiliation in closed marginal groups was practiced. Cranial deformation is the dynamic distortion of the normal vectors of the infantile neurocranial growth through the agency of the externally applied forces. It was practiced in every continent in the past. Such cranial deformation could have been intentional or unintentional. Intentional cranial deformation is especially linked to group affiliation and social supremacy in closed marginal tribal societies.[17,18] Such cranial elongations to have longer conical skulls provide a special supremacy to rule over others in terms of then prevalent cultural rituals and beliefs. Thus such prolonged efforts to alter the cranial structure may lead to the presence of transverse suture and formation of Inca bone in the progeny of Inca tribes.

The formation of Os Inca totum has embryological and oesteological viewpoints. The portion of the occipital bone inferior to superior nuchal line ossifies in cartilage whereas superior portion ossifies in membrane. A common but oversimplified account of occipital ossification states that above the highest nuchal line, the squama develops in a fibrous membrane and ossifies from two centers, one on each side from the second fetal month; this part may remain separate as interparital bone. The rest is preformed in cartilage below the highest nuchal lines, the squama ossifies from two centers appearing in the seventh week and then soon unites; these two regions of squama unite in the third post natal month but the line of union is recognizable at birth. In the cartilaginous supra occipital part, five endochondral centres, a pair each for right and left lateral segments and one for the central segment (Kerckring's Centre) appears. The formation of Inca bone is caused because of failure of fusion of interparital bones formed by primary ossification centers.[4,7,8,11]

Some researchers proposed that the membranous or dermal part above the nuchal lines as compounded of interparital and pre-interparital parts; the interparital consisting of two lateral plates and a central piece. The intra membranous centres proposed for these are a pair for each lateral plate and two for the central piece, additionally a pair of centres for pre interparital bone,[6,7] while other researchers have stated that the pre interparital elements are sutural. But much uncertainty still persists regarding the status of these accessory ossicles. Fusion may fail, partly or completely, between any of these elements. [4]

The earlier studies based on secondary data, in Central and South Asian Region showed the frequency distribution of os Inca totum to be 0.0325, 0.0317, 0.0081, 0.000, 0.0228, 0.0 in Tibetan and Nepalese, Assamese and Sikkimese, East Indian, South Indian, Northwest Indian and Kazakhs population respectively.[12] In one of the study conducted in the central India region in 92-94, gross incidence of Inca bone was found to be 1.315 %. Incidence rate was higher in male skulls than female skulls (male: 1.428%; female: 1.176%). The Inca bones frequently occurred singally. Out of the five observed Inca ossicles, two were fragmented. [12, 19]

Some researchers have established the co-occurance of wormian bones with Inca bones in same skull than those without it. This resembles with findings of the present case which is also associated with wormian bones. Among modern population, the frequency of Inca bone is highest in marginal isolates, those who have retained traits of early ancestral population.[1] Inca bone is considered to be regional character of East-Asians providing evidence of regional continuity. Such occurrence of Inca bone has paleoanthropological, morphological, medicolegal and evolutionary importance.

Fig. I: Showing Os Inca Totum

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Case Report

Bilateral Multicystic Dysplastic Kidneys in Association with High Ano-Rectal Anomaly - A Case Report

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Abstract:

Multicystic dysplastic kidney disorder (MCDK) is commonly sporadic but is rarely an inherited congenital disease. It is the commonest cause of abnormally enlarged kidney, diagnosed on antenatal ultrasound examination. It is typically a unilateral disorder; bilateral condition is incompatible with extra uterine life. Association of this disease with abnormalities of various organs is common . We report a rare case of bilateral multicystic dysplastic kidney associated with high ano-rectal anomaly which was diagnosed antenatally and pregnancy was terminated.

Key Words: Ano-rectal anomaly, Bilateral, Multicystic dysplastic kidney

Introduction:

Renal dysplasia is a developmental disorder and is categorized as either hypoplastic dysplasia, multicystic dysplasia, agenesis, segmental agenesis or congenital hydronephrosis with or without dysplasia. Multicystic dysplastic kidney (MCDK) is the most common dysplasia variant. [1] It is typically a unilateral disorder.[2] Involvement of other organs is likewise common in patients with MCDK. Esophageal atresia, tracheoesophageal atresia, ventricular septal defect, and patent ductus arteriosus are the most common extrarenal abnormalities.[3] The widespread use of prenatal sonography has led to early discovery of multicystic kidneys.[4] In the present case report, a rare occurrence of bilateral MCDK with associated ano-rectal anomaly is discussed.

Case Report:

A 23 year old female presented at 26 weeks of gestation for a routine antenatal check up. She was G1 P0. Prenatal ultrasonography showed small for date fetus with severe oligohydramnios and multiple congenital anomalies (absent stomach bubble, bilateral multi cystic kidneys, megabladder, dilated bowels). The couple had non consanguineous marriage with no history of congenital anomalies in her or husband's family. The family was distressed and opted for termination of pregnancy. A still born male fetus weighing 600gms was delivered vaginally after induction with Mifepristone and Dinoprost gel. The fetus was sent in formalin to the pathology department.

The fetus in formalin was received in Pathology department after 2 days of delivery. The fetus was showing signs of maceration and was small for gestational age (by anthropometry). The fetus had low frontal hair line, prominent epicanthal folds, bilateral low set and posteriorly rotated ears, flattened nasal tip and micrognathia (Fig. IA). The testes were undescended and the urethral meatus was patent. There was only a dimple present at the site of anus (Imperforate anus; Fig. IB). The rest of the external examination was normal.

As per the parent's wish, the autopsy was immediately carried out and fetus was returned for ritual and final disposal.

The internal examination revealed an enlarged bladder, bilateral multicystic kidneys and dilated rectum (Fig IC).

The kidneys were asymmetric (right kidney was larger than left) with maintenance of reniform shape and presence of multiple cysts on the surface (Fig. IC). Cut section showed presence of multiple cysts with loss of corticomedullary demarcation. Histopathological examination showed features of bilateral multicystic dysplastic kidneys (Fig II).

The left ureter was hypoplastic. The right ureter in the distal one third was dilated (Hydroureter). The bladder showed marked hypertrophy with absence of posterior urethral valves.

There was rectal agenesis with dilatation of

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Fig I: (A) Shows dysmorphic facies. (B) Shows imperforate anus. (C) Shows bilateral multicystic kidneys with hypoplastic left ureter, megabladder and dilated rectum.

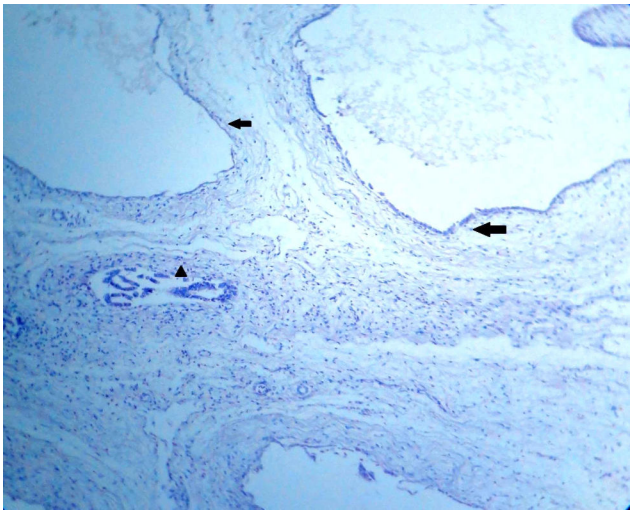

Fig II: Histopathological picture of MCDK showing multiple cysts lined by flattened epithelium with (⬅) few primitive tubules (▲; H & E, 40X).

proximal rectum which ended as a blind pouch and was attached by a thin strand to the posterior wall of bladder (Fig. IC).

The left lung was hypoplastic with a single lobe and a partial fissure. Microscopically, features of hypoplasia could not be determined because of autolysis. The spleen and adrenals showed autolysis with presence of cysts on microscopy. The other organs were normal.

In view of above anomalies, parenteral karyotyping was advised.

Discussion:

Multicystic dysplastic kidney is a congenital renal malformation characterized by the presence of multiple cysts in dysplastic kidneys. It is a form of renal dysplasia, where cystic elements are found in the kidney along with immature, undifferentiated primitive tissue. Embryologically, MCDK may result from abnormal renal morphogenesis.[1] Multicystic disease of the kidney is typically a unilateral disorder.[2] Bilateral MCDR malformations are frequently associated with the fatal Potter anomaly.[1] The sequence, as described by Potter in association with renal agenesis with oligohydramnios, bilateral pulmonary hypoplasia and immature lungs microscopically may result in still birth and neonatal death.[5] Some of the features of Potter sequence found in the present case were oligohydramnios, dysmorphic facies (prominent epicanthal folds, flattened nasal tip and low set and posteriorly rotated ears) and grossly hypoplastic lungs. Bilateral MCDK was found in the present study. Similar findings were reported by various authors.[6-10] The majority of dysplastic kidneys are associated with urinary tract obstruction commencing in early embryonic life.[11] The type and severity of renal dysplasia depends on the pattern of malformation and severity of urinary tract obstruction.[9] In the present case, the fetus had hypertrophied bladder in the absence of posterior uretheral valves, which implies some obstruction in the lower urethra, which were not included during en-bloc removal of organs during autopsy. This obstruction might be the cause for bilateral MCDK. Similar finding of bilateral MCDK with urinary tract obstruction was also found in 2 cases.[9]

Involvement of other organs is likewise common in patients with MCDK. Esophageal atresia, tracheoesophageal atresia, ventricular septal defect, and patent ductus arteriosus are the most common extrarenal abnormalities.[3] In the present case associated rectal agenesis and imperforate anus was found. Similar such association (MCDK with dysplastic empty scrotum and anal atresia) was also found in one case study.[7] In a study of unusual associations with anorectal malformations in 284 children, one case was found to have MCDK.[12]

Correct and timely antenatal diagnosis of bilateral MCDK with associated fetal anomalies is important so that proper counselling and appropriate obstetric management can be extended. Antenatal diagnosis is facilitated by ultrasonography that gives a characteristic picture at 24-28 weeks.[2] In the present case, antenatal diagnosis of bilateral multicystic disease was made at 26 weeks and pregnancy was terminated.

Conclusion:

Routine antenatal scans are done to detect the anomalies in fetus, some of which may be incompatible with life. Performing autopsies on such fetuses can result in confirmation of ultrasonographic findings and finding out other associated anomalies or related syndromes. This can aid the obstetrician in planning for appropriate management.

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Case Report

SingleVisit Apexification Technique for Inducing Root-End Barrier Formation in Apical Closures: Report of Two Cases

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Abstract:

Traumatized tooth rendered nonvital (pulpal necrosis) before the final stage of the root development results in a short root with a wide canal that can be either divergent or parallel. Although the root canal therapy is the choice of treatment for a nonvital tooth, the above mentioned abnormal root anatomy does not permit a predictable outcome. Mainly, it is not feasible to achieve a good apical seal due to lack of constriction in the open apex and a good lateral seal due to an abnormal width and shape of the root canal. Numerous procedures and materials have been utilized to induce root-end barrier formation. Mineral trioxide aggregate (MTA) reacts with tissue fluids to form a hard tissue apical barrier. As a result, MTA shows promise as a valuable material for use in single-visit apexification treatment, primarily for treating immature teeth with necrotic pulp. Here, we present two cases being successfully treated in a single visit apexification with MTA followed by endodontic treatment.

Key Words: apical closures, MTA, root end barrier formation, single-visit apexification, tooth trauma.

Introduction:

Dental caries and trauma are the most common challenges to the integrity of a tooth as it matures. Both insults can render the dental pulp nonvital. If this occurs prior to complete root formation and apical closure, normal root development is halted. Clinically, there are several conditions associated with treating teeth that have a widened or open apical foramen. For one, the apical diameter of the canal is often larger than the coronal diameter, so debridement is difficult. In addition, the lack of an apical stop makes obturation in all dimensions virtually impossible. Finally, the thin walls of the root canal are prone to fracture, so that surgical treatment is generally not a viable option[1].To avoid these complications, apexogenesis i.e. vital pulp therapy is indicated to encourage continued physiological development and formation of the root end .When the insult to the tooth has caused pulpal necrosis, alternative treatment modality that is apexification must be considered. The American Association Endodontist's Glossary of endodontic terms refers to apexification as "a method of inducing a calcified barrier in a root with an open apex or the continued apical development of an incompletely formed root in teeth with necrotic pulp."

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Nonvital immature teeth require apexification prior to nonsurgical root canal treatment. Numerous procedures utilizing various materials have been recommended to induce root-end barrier formation. These include: no treatment,[2] infection control,[3] induction of a blood clot in the periradicular tissues,[4] antibiotic pastes,[5] and calcium hydroxide mixed with various materials.[6]

Since its first description in the dental literature by Lee et al[7] in 1993, and its first use as root end filling material,[8] the development of Mineral Trioxide Aggregate (MTA) material was truly a landmark event in dentistry and in endodontics in particular. This event dramatically increased the success rate of many cases that used to have high failure rates. Many advantages of MTA material enlarged its use markedly in different fields of dentistry, from which, endodontics was the largest field to take advantage of this material.

Mineral Trioxide Aggregate is a powder consisting of fine hydrophilic particles of tricalcium silicate, tricalcium aluminate, tricalcium oxide and silicate oxide. It also contains small amounts of other mineral oxides, which modify its chemical and physical properties. Hydration of the powder results in formation of colloidal gel that solidifies to form a strong impermeable hard solid barrier in approximately three to four hours. Electron probe microanalysis of MTA powder showed that calcium and phosphorus are the main ions present.[9] Bismuth oxide powder has been added to make the aggregate radio-opaque. Mineral trioxide aggregate has a pH of 12.5 after setting, similar to calcium hydroxide. This may impart some

antimicrobial properties.[10] The material has a low solubility and a radio-opacity slightly greater than that of dentin. Because it has low compressive strength[9], it should not be placed in functional areas.

Case report 1:

An 18 year old female patient was referred to the Department of conservative dentistry with the chief complaint of spontaneous pain, the intensity of which increased on mastication. She had a history of trauma at the age of around 12 years but remained asymptomatic till recently.

Clinical examination revealed deep carious lesion involving the pulp of the concerned tooth 44. The tooth was tender on percussion and there was a mild pain on palpation. Labial mucosa adjacent to the concerned tooth was inflammed.

Intraoral periapical radiograph using radiovisiography (Kodak 5100, France) revealed short root. It also showed a blunderbuss open apex with thin dentinal walls of tooth 44. Small area of periradicular lesion associated with the root apex of the tooth 44 was also evident (Fig.I).

Pulp testing with an electric pulp tester (Parkell Inc. USA) and thermal test using hot gutta percha elicited non-responsiveness from the suspected tooth when compared to the control teeth. No signs of mobility or periodontal pockets were present. The diagnosis of pulpal necrosis with symptomatic periradicular Periodontitis was made.

The patient was discussed with various treatment plans and consent was obtained. Following isolation with a rubber dam, an endodontic access opening was made under magnification of an operating microscope (20X Seiler precision microscope, USA). The root canal was copiously irrigated with 5.2% sodium hypochlorite and 17% EDTA solution. Working length was determined by Root ZX^{R}. The root canal was cleaned and shaped by rotary nickel-titanium ProTaper instruments to the size F5. Calcium hydroxide paste (Ultracal, Ultradent, South Jordan, UT) was placed as an intra-canal medicament and the access cavity was temporized (Cavit G^{TM}). The patient was recalled 1 week later. On recall visit, the tooth was asymptomatic. The temporary restoration was removed and was irrigated with normal saline and dried. Once cleaning and shaping was completed, a plugger size 40 (generally used for warm vertical compaction) fitted loosely within 1.5 mm from the apex of the root canal system was selected. A thick mix of MTA and distilled water was prepared and then placed in the middle to apical third of the root canal system using an MTA gun (Fig. II). Mineral trioxide aggregate was compacted with the plugger previously fitted to the root canal system. Care was taken to prevent extrusion of the material into the

Fig. I: Preoperative radiograph of tooth 44 revealed short root with blunderbuss open apex and thin dentinal walls.

Fig.II. Mineral trioxide aggregrate plug.

Fig.III. Post obturation radiograph.

periradicular area. The final adjustment was done with the light force using the butt end of sterilized greater taper paper points (Dentsply Maillefer) with the aid of the radiograph, leaving a minimal thickness of 6 mm. Once the MTA layer is adequately compacted to the working length and confirmed with a radiograph, the excess was removed from the coronal third of the canal system by irrigation with sterile water. The remaining fluid is removed with sterile paper points. A moist cotton pellet was placed against it, as the presence of moisture is essential for the material to set. The access cavity was temporized. The patient was recalled after 24 hours. At the next appointment, the MTA felt hard to an endodontic explorer DG-16 (Hu-Friedy International). The remaining part of the root canal was back-filled with injection molded thermoplastic gutta-percha (Obtura II, USA) and sealer (AH 26, Dentsply, Germany). Post obturation radiograph was taken which showed well obturated root canal (Fig. III). The patient was asked to report after a week for clinical evaluation and the post endodontic restoration.

During recall, the tooth was asymptomatic and post endodontic composite (Clearfil Majesty™, USA) restoration was placed and patient was recalled after six month for the follow-up.

Case report 2

A 14 year old boy was referred to the Department of conservative dentistry with the chief complaint of pus discharge from the openings near the root apices of tooth 11 and 21. He had a history of trauma due to fall two and half years back.

Clinical examination revealed fractured tooth 11 and 21 involving the pulp. Sinus opening was present near the root apices of both the central incisors. The teeth were not tender on percussion and there was no pain on palpation. Labial mucosa adjacent to the concerned teeth was inflammed.

Intraoral periapical radiograph using radiovisiography revealed blunderbuss open apices with thin dentinal walls of tooth 11 and 21. Small periradicular lesions was evident associated with the root apices of the tooth 11 and 21(Fig. IV).

The options for root-end management include classic apexification with long term Calcium hydroxide to induce formation of an osteodentin apical barrier, or single visit apexification with the placement of an artificial apical plug or barrier of MTA or periapical surgery with placement of a root-end filling, were discussed. The patient agreed and gave his consent for single visit apexification using MTA.

The inherent difficulties of inducing barrier formation over a period of months are avoided when treatment is completed in one appointment. Such treatment could be described as a single visit root-end barrier formation in apical closure with MTA. When MTA is used in this manner, it becomes the final obturating material in the apical to middle third of the canal system.

Following isolation with a rubber dam, an endodontic access opening was made for tooth 11 and 21 under magnification of an operating microscope. The root canals were copiously irrigated with 5.2% sodium hypochlorite and 17% EDTA solution. Working length was determined by Root ZX^{R} (J. Morita Corporation, Kyoto, Japan).

Calcium hydroxide paste was placed as an intra-canal medicament and the access cavities were temporized (Cavit G™, 3M ESPE, Seefeld, Germany). The patient was recalled 1 week later. On recall visit, the tooth was asymptomatic. The temporary restoration was removed.

A thick mix of MTA and distilled water was prepared and then placed in the middle to apical third of the root canal system using an MTA gun (Fig. V). Mineral trioxide aggregate was compacted with the plugger previously fitted to the root canal system .Care was taken to prevent extrusion of the material into the peri-radicular area. The final adjustment was done with the light force using the butt end of sterilized greater taper paper points (Dentsply Maillefer) with the aid of the radiograph, leaving a minimal thickness of 6 mm. Once the MTA layer was adequately compacted to the working length and confirmed with a radiograph, the excess was removed from the coronal third of the canal system by irrigation with sterile water. The remaining fluid was removed with sterile paper points. A moist cotton pellet or paper point was placed against it, as the presence of moisture is essential for the material to set. The access cavity was temporized (Cavit-G). The patient was recalled after 24 hours. At the next appointment, the MTA felt hard to an endodontic explorer DG-16. The remaining part of both the root canal was back-filled with injection molded thermoplastic gutta-percha (Obtura II,Obtura Corporation, Fenton, USA) and sealer (AH 26, Dentsply, Germany). Post obturation radiograph was taken which showed well obturated root canal (Fig. VI). The patient was asked to report after a week for clinical evaluation and the post endodontic restoration.

During recall, the tooth was asymptomatic and post endodontic composite (Clearfil Majesty™ posterior Kuraray America, NY, USA) restoration was placed and patient was recalled after six month for the follow-up.

Fig.IV Preoperative radiograph of teeth 11 and 21 revealed blunderbuss open apex and thin dentinal walls and small periradicular rarefaction.

Fig.V Mineral trioxide aggregrate Apical plug with 11 and 21.

Fig.VI: Post obturation radiograph.

Discussion:

Any extended treatment plan runs the risk of losing the patient due to geographical reasons. If a child moves during the course of treatment, it is difficult to ensure that dressing changes will be made as necessary until a barrier is formed. Repeated clinical visits can be disruptive and difficult to maintain. These appointments are also easy to forget, since the patient has little discomfort and the tooth looks normal clinically. Children may be more traumatized by apexification treatments that require repeated visits, and it is these younger children with very wide apices that often need extended treatments. Thus, the need for a reliable one-visit apexification treatment is evident. Most commonly, the apexification procedure has been performed utilizing calcium hydroxide. In 1959, Granath was the first to describe the use of calcium hydroxide for apical closure.[11] Prior to this, nonvital immature teeth were often extracted.[12] Frank popularized the technique in which the canals are debrided, Calcium hydroxide is mixed with camphorated *p*-chlorophenol to make a paste that is then placed into the canals, and the access opening is subsequently filled.[6] In this procedure, the calcium hydroxide dressing is replaced every three months until a barrier is formed, which may require up to 24 months. When this procedure is performed today, the calcium hydroxide is most commonly mixed with sterile water or an anesthetic, but the time for barrier formation remains the same.[13]

Unfortunately, the Frank's technique sometimes provides inconsistent results due to: 1) The periapex closes with a definite (though minimal) recession of the root canal. The apical aspect continues to develop with a seemingly obliterated apex. 2) The obliterated apex develops without any change in the root canal space. 3) A thin, calcific bridge that is not radiographically discernable develops. 4) A calcific bridge forms just coronal to the apex and can be determined radiographically. Other inconsistencies relating to the use of calcium hydroxide for apexification include the time for root apices to close, the number of dressings necessary to complete closure, and the role of infection. Depending on the study, the speed of barrier formation varies from 3 to 24 months.[6,14] There are also variations in the recommended number of reapplications of calcium hydroxide.[14-18] Reapplication at 1 month then 3 months, or 1 month then 6 to 8 months has been suggested until apical barrier formation occurs.[16] Finally, some studies have reported an increase in the time for apexification when

infection is present,[19,20] while others have demonstrated no statistically significant differences.[17,18,21]

These conflicting reports aside, the procedure for treating teeth with open apices is a difficult one. The root walls are thin and fragile, which render the tooth more susceptible to fracture during compaction of the obturation material.[1] Since patients are generally young, surgery is not a desirable course of treatment because immature teeth have large, patent dentinal tubules and a root-end filling may not provide an optimal seal. Compaction of a root-end filling may also cause fracture of the thin dentinal walls. Another factor that may compromise long- term apexification is the difficulty in maintaining a temporary filling that adequately seals the access opening. A temporary filling 4 mm in thickness is required to create a suitable seal. If there is dilution and/or contamination of the paste during the apexification treatment, with exposure of the healing tissues to bacteria, then acute exacerbation and a delayed healing response may occur.[6]

Hence in the present cases a non surgical,single visit apexifecation using Mineral trioxide aggregate was performed. An artificial apical plug or barrier of MTA was placed followed by the endodontic treatment.

Torabinejad et al performed a series of biocompatibility studies with MTA.[23] Kettering & Torabinejad found it to be non mutagenic,[22] and Torabinejad et al found it to be less cytotoxic than SuperEBA and IRM.[23] In animal studies, MTA was the only material studied that allowed cementum overgrowth. [24,25] It was found to be biocompatible when implanted into guinea pigs,[26,27,28] dogs[24] and monkeys,[25] and was more biocompatible than amalgam, Super EBA or IRM. In vitro studies of human osteoblasts showed that MTA stimulated cytokine release[29] and interleukin production.[30] These studies suggest that MTA is not just an inert material but may actively promote hard tissue formation.

Torabinejad et al tested MTA, amalgam, ZOE and SuperEBA against nine facultative bacteria and seven strict anaerobes.[10] Mineral trioxide aggregate was found to have an antibacterial effect on five of nine facultative bacteria but no effect on any of the strict anaerobes. The other materials had similar effects. The researchers concluded that none of the test materials had all of the antibacterial effects desired for a root-end filling material. Since the present case had an acute infection hence MTA was used owing to its antibacterial properties.

Shabahang et al compared MTA, osteogenic protein- 1 and Calcium hydroxide for apexification in dogs.[31] They found that MTA induced hard-tissue formation more often than did the other test materials and concluded that MTA was suitable for use as an apical barrier for apexification in immature roots..

In preparing the site to receive the MTA, the clinician should follow several guidelines. All irrigation should be performed before the MTA is placed. Any irrigation after placement will cause significant washout of the material. The preparation or resorptive defect does not have to be perfectly dry, but most of the fluid should be removed. If MTA is placed from inside the tooth, a moist cotton pellet or paper point should be placed against it, because the presence of moisture is essential for the material to set. The access cavity is then closed. MTA requires several hours to set into a hard mass. Most internal repairs with MTA require a second visit to complete the root canal therapy or restoration.

In the present case report all the guidelines for the placement of MTA were followed.

Blood contamination of the root-end site during barrier formation is also a relevant concern. In a similar comparative study, investigators noted that the presence of blood did not affect MTA's ability to maintain a seal.[32] Holland et al theorized that the tricalcium oxide in MTA reacts with tissue fluids to form calcium hydroxide, resulting in an apical barrier.[33] In addition, apexification implies the presence of a necrotic pulp, so a material with antibacterial properties is also desired. Several studies have evaluated the ability of MTA to kill bacteria. In a comparison study of root-end filling materials and their effects on nine facultative bacteria and seven strict anaerobic species, MTA had an antibacterial effect on some of the former, but no effect on the latter.[23]

Irregular dentinal walls and divergent apices make the adaptation of MTA more difficult. In this case, the access cavity was widened to enhance the visibility of the root and provide straight access to the apices of the tooth. The procedure should be done with caution. The orthograde placement of the apical plug is more sensitive than the retrograde method. Hachmeister et al also found that the sealing ability of MTA is superior when used as an orthograde plug[34].

In the present case the plugger size 40 fitted loosely within 1.5 mm from the working length. With this plugger the MTA was applied to the walls of the root canal

system and the final adjustment was done with light force using the back end of sterilized paper points with the aid of the radiograph. Care was taken to prevent extrusion of the material in to the periradicular area.

The procedure of apexification often requires special instrumentation and the improved visualization. Hence, in the present case reports illumination and magnification was achieved by using an operating microscope (20X Seiler precision microscopes, St.Louis, MO, USA).

Hachmeister et al emphasized that the apical plug thickness may only have a significant impact on displacement resistance[34] while in the present case the thickness of apical plug of MTA was 6 mm and the remaining part of the root canal was back-filled with injection molded thermoplastic gutta-percha (Obtura II, USA) and sealer (AH 26, Dentsply, Germany).

Conclusion:

The development of Mineral Trioxide Aggregate (MTA) material by Torabinejad was truly a landmark event in dentistry and in endodontics in particular. The use of MTA changed dramatically the treatment plan and increased the success rate of many previously thought of as hopeless cases. MTA is an efficient and promising dental material. The many advantages of MTA enlarged its use markedly in different fields of dentistry, from which, endodontics was the largest field to take advantage of this material. MTA's approval in 1998 by the U.S. Food and Drug Administration should lead to more widespread use. The material appears to be an improvement over other materials for some endodontic procedures that involve root repair and bone healing. Although these potential concerns must be addressed and considered, the potential advantages of single-visit apical closure with MTA outweigh any negatives. As previously discussed, one-visit treatment is always advantageous over multiple treatments that may occur over many months. Another positive aspect is that MTA provides scaffolding for the formation of hard tissue and the potential of a better biological seal. When obturation finally occurs following hard tissue deposition with Calcium hydroxide, the clinician can never be sure of the integrity of the barrier. Single-visit apical closure with MTA avoids many of the pitfalls of traditional treatment methods. It is a viable option for treating immature teeth with necrotic pulps and should be considered as an effective alternative.

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Case Report

Management of a Large Periapical Cyst: A Case Report

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Abstract:

Traumatic injuries commonly affect the anterior teeth leading to slow death of the pulp. This may give rise to a periapical or radicular cyst which results from the proliferation of cell rests of Malassez following pulpal necrosis of a non-vital tooth. This condition is usually asymptomatic but can result in a slow-growth tumefaction in the affected region. On radiography the lesion can be seen as a round or oval, well circumscribed radiolucent area involving the apex of the infected tooth. Nonsurgical management should be the treatment of choice of a periapical cyst. However, periapical surgery can be considered, if the lesion is extensive and fails to respond to a nonsurgical approach.

Key Words: Dental pulp necrosis, Non-vital tooth, Radicular cyst, Surgical cyst enucleation.

Introduction:

A periapical or radicular cyst arises from epithelial cell rests of Malassez which proliferate by an inflammatory process originating from pulpal necrosis of a non-vital tooth. This condition is usually asymptomatic but can result in a slow-growth tumefaction in the affected region.

Bhaskar[1] and Shear[2] reported that the incidence of radicular cysts is found to be highest among patients in their third decade of life and greater among men than women. Shear[2] also reported that they have particularly high incidence in the maxillary anterior region, presumably as a result of trauma. A case report is presented of an individual with a large radicular cyst.

Case Report:

A 23 year old male patient reported to the Department of Conservative Dentistry & Endodontics, People's College of Dental Sciences & Research Center, Bhopal with the chief complaint of pain and swelling in the upper front teeth region of jaw. He gave a history of trauma 15 years back for which no treatment was sought. Post trauma, he had pain in relation to maxillary central incisors which subsided after 1 week on its own. He gave a history of swelling along with pus discharge from gums since last 2 years. On clinical examination, 21 was found to be discolored (Fig. Ia) and a diffuse palatal swelling (Fig. Ib) of approximately 3 x 2 cms in size, extended 2 cms on the left and 1 cm on the right from the midline of the palate. Anteroposteriorly, it extended 0.5 cm from the incisive papilla to 2 cms posteriorly. The swelling was tender and fluctuant on palpation.

Vitality test gave a negative response in relation to 11 and 21. An Intra Oral Periapical Radiograph (IOPA) in relation to 11 & 21 (Fig. IIa) and Occlusal view radiograph of the maxilla (Fig. IIb) revealed large well defined periapical radiolucency involving central incisors and an open apex in relation to 21. On FNAC, about 0.8 ml of straw colored, shimmering fluid, serous in consistency was aspirated and sent for cytological examination which revealed numerous cholesterol crystals and RBCs along with few inflammatory cells.

On the basis of clinical, radiological and cytological examination, a provisional diagnosis of Radicular cyst was made. Differential diagnosis included Nasopalatine cyst, Median palatal cyst, Traumatic bone cyst, and Globulomaxillary cyst.

An endodontic therapy was planned with respect to 11 & 21. Patient became extremely apprehensive whenever an effort was made to apply rubber dam, which contraindicated its usage. Repeated calcium hydroxide dressings were given at an interval of 5 days for 1 month. However, there was continuous fluid drainage through the canal of 21; hence surgical enucleation of the cyst (Fig. IIIa, b) through a buccal approach was adopted, full thickness flap was raised. Cystic fluid was clearly visible through the perforation. Cyst enucleation was carried out in toto. Enucleated cystic lining (Fig. IVa) was sent for histopathological examination which revealed 6-7 cell layered thick, non keratinized stratified squamous epithelium. Connective

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Fig. I: a) Discolored 21, b) Diffuse palatal swelling.

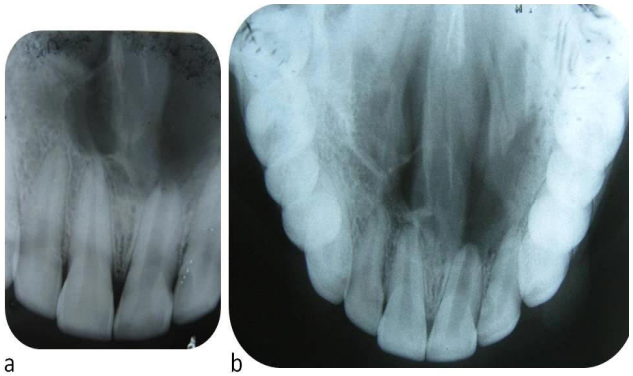

Fig. II: Preoperative IOPA in relation to 11 & 21, b) Occlusal view radiograph of the maxilla.

tissue capsule showed the presence of cholesterol crystals along with acute & chronic inflammatory cells which confirmed the diagnosis of an Infected Radicular cyst (Fig. IVb). Absorbable Gelatine Sponge (ABGEL) a haemostatic agent was placed in the cystic cavity and flap was secured in position with sutures. After 1 week the sutures were removed. A marked reduction in palatal swelling could be appreciated after one month.

Non vital / Walking bleach using a mixture of hydrogen peroxide and sodium perborate was done in relation to 21 with a successful outcome and aesthetically pleasing patient smile (Fig. Va, b).

At the end of one year, palatal swelling subsided completely. An Intra Oral Peropical Radiograph in relation to 11 and 21 (Fig. VIa) and Occlusal view radiograph of the maxilla (Fig. VIb) showed marked reduction in the size of radiolucency appreciating post operative healing.

Discussion:

The periapical cyst is the most common odontogenic cyst (52.3-70.7 percent) followed by the dentigerous cyst (16.6-21.3 percent) and odontogenic keratocyst (5.4 - 17.4 percent).[3] The choice of treatment may be determined by factors such as the extension of the lesion, relation with noble structures, evolution, origin, clinical characteristic of the lesion, systemic conditon and cooperation of the patient.[4]

The treatment of these cysts is still under discussion and many professionals opt for a conservative treatment by means of an endodontic technique.[5,6] However, in large lesions the endodontic treatment alone is not sufficient and it should be associated with decompression or marsupialisation or enucleation.[7]

In the present case, endodontic treatment was carried out in multiple visits with interim calcium hydroxide dressings. The use of root canal dressings between sessions in root canal treatment of teeth with chronic periapical lesions is important for reducing levels of bacteria better than that obtained with mechanical preparation, particularly by penetration of areas that are unreachable by instruments or irrigation solutions, such as dentinal tubules and ramifications. Calcium hydroxide has also shown clinical efficiency in reducing exudate due to its hygroscopic properties. Studies have shown that at least 2 weeks are necessary for calcium hydroxide bactericidal activity.[8]

Calcium hydroxide intracanal medicament created a more favourable environment leading to healing of periapical lesion in the right central incisor which was obturated by lateral condensation using zinc oxide eugenol sealer and gutta percha before the surgery. The periapical lesion on the left side, however, did not respond to the intracanal medicament because of the causative factor being located beyond the root canal system, viz., within the inflamed periapical tissue, thus requiring surgical intervention. After the surgery a plan for long term treatment of 21 with intracanal medicament was made. Metapex (Calcium hydroxide with Iodoform, META BIOMED CO. LTD) was used this time. At the end of 6 month follow-up, patient was free from all symptoms and signs with optimum tissue healing. Radiographic examination revealed a decrease in the size of periapical radiolucency bilaterally. Tooth 21 was obturated using Inverted cone technique and lateral condensation of gutta percha with zinc oxide eugenol sealer. A definite apical stop could be felt at the end of canal during obturation.

By filling the canal with calcium hydroxide, a physical barrier is created that prevents migration of multipotent undifferentiated mesenchymal cells into the canal and regeneration of tissues at the lateral dentinal walls.[9] Moreover, use of Calcium hydroxide medicaments for apexification is cost effective when compared to other materials like Mineral Trioxide Aggregate.

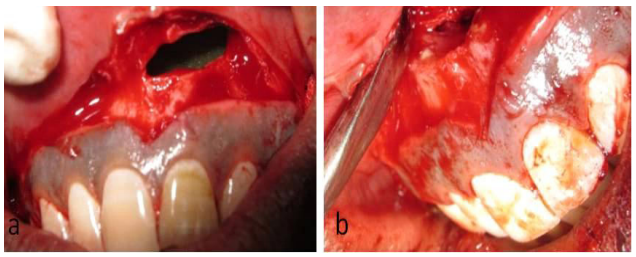

Fig. III:. a) Cystic fluid visible through the perforation, b) Cyst enucleation.

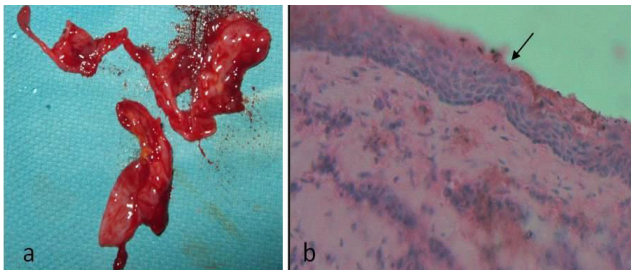

Fig. IV: a) Enucleated cystic lining, b) Photomicrograph showing 6-7 cell layered thick non keratinized stratified squamous epithelium (H & E stain, 400 X).

Fig. V: a) After Non Vital Bleaching in relation to 21, b) Aesthetically pleasing patient smile.

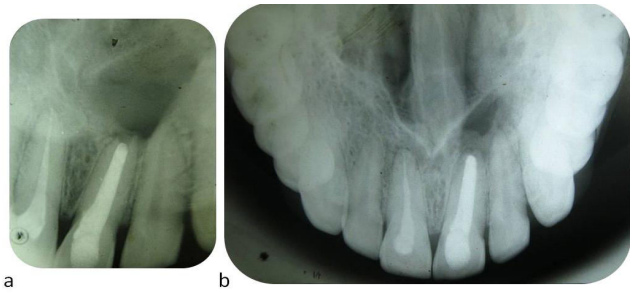

Fig. VI: a) IOPA in relation to 11 & 21, b) Occlusal view radiograph of the maxilla after a follow up of 1yr

In this case, a root end resective procedure followed by retrograde filling would have resulted in a compromised crown root ratio, thereby excluding it from the treatment plan. Thus a maximum cemental covering on the root surface and original root length to help tooth stability could be maintained. Frank[10] reported the treatment of 3 cases based on the normal physiologic pattern of root development that brings about the resumption of apical development so that the root canal can be obliterated by conventional lateral condensation techniques. Likewise, the technique described here brings about an interesting phenomenon: The interrupted process of apical development continues to its potential, subsequently allowing for the obliteration of the root canal by routine endodontic procedures. The role of the epithelial sheath of Hertwig in root formation has been well established. The fact that root formation can be resumed after a period of inactivity caused by infection, leads to the assumption that epithelial rests of Malassez, which are the remnants of Hertwig's sheath, persist throughout life and resume their function of cementum deposition resulting into obliteration of root apex, once the source of infection has been removed. Considering patient's young age and good health, bone graft was not used. This case is a good example of a large lesion been treated with conventional RCT and cyst enucleation without the use of materials which enhance bone regeneration like Platelet Rich Fibrin (PRF) G-bone (Synthetic Granules and blocks made of Multiphasic Calcium Hydroxyapatite in low crystalline form).

Conclusion:

The clinical case reported was managed successfully by endodontic therapy with emphasis on thorough debridement and disinfection of the root canal system which was followed by surgery. The authors recommend non surgical management of large periapical lesions in view of clinical evidence present. However in specific situations where the size and extent of the lesion is of critical importance, surgery is a viable option with good prognosis. An endodontist should have thorough knowledge about materials and various treatment options involved in management of such a case.

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Case Report

Femoral Neuropathy After Vaginal Hysterectomy Under Spinal Anaesthesia : A Rare Case Report

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Abstract:

The femoral nerve is the largest branch of the lumbar plexus and arises from the posterior branches of L2 to L4 roots. Femoral neuropathy after pelvic operation has occasionally been reported in the literature, but femoral neuropathy after vaginal hysterectomy is very rare. The possible causes of femoral neuropathy include overtraction of the femoral nerve during surgery, direct compression of the femoral nerve by the surgical instrument, or entrapment of the femoral nerve at the inguinal ligament. This report describes a case of bilateral femoral neuropathy after hysterectomy and discusses the anatomic relations of the femoral nerve, possible mechanism of injury, diagnosis, management, and measures for prevention.

Key Words: Femoral nerve ,lithotomy,spinal anaesthesia,vaginal hysterectomy.

Introduction:

Vaginal hysterectomy is one of the common elective surgeries performed by the gynaecologist. The most common indication of patient undergoing such surgery is genital prolapse. For the anesthesiologist the most feared complication of regional anesthesia is a neurologic deficit. Fortunately, neurologic deficits are very rare. Lithotomy is the second most common surgical position[1]. Lithotomy is the most extreme of the supine position. Positioning the patient in lithotomy has a great risk for causing injury to patient, if not performed appropriately. Femoral neuropathy after pelvic operation has occasionally been reported in the literature, but femoral neuropathy after vaginal hysterectomy is very rare, with only 29 cases reported in the literature[2].

We here by report a case in which improper lithotomy position for prolonged duration resulted in postoperative femoral neuropathy in a patient who underwent vaginal hysterectomy.

Case Report:

A 60years old female patient weighing 50kg having third degree uterovaginal prolapse was posted for vaginal hysterectomy and pelvic floor repair. History and clinical examination were unremarkable,and her other investigations were within acceptable limits. She was hypertensive, and was on Tab.Atenolol 50mg OD; her blood pressure was within normal limits. On the day of surgery she was preloaded with IV 500ml Ringer's lactate. She was premedicated with Inj.Ranitidine 50mg and Inj.Ondansetron 4mg IV. All mandatory monitors were attached and subarachnoid block was achieved with 3.6 ml of 0.5% Inj. Bupivacaine heavy in sitting position. Patient was put in supine position, her highest sensory level was at T_6 with complete motor block i.e. Bromage grade III.Patient was given lithotomy position for vaginal hysterectomy with her knees and hips flexed on swing stirrups. During the procedure patient was given sedation with Inj.Midazolam1mg and Inj.Pentazocin 15mg. She received 1000ml of Ringer's lactate and 500ml of Dextrose normal saline. During surgery, her intraoperative vitals were within normal limits.Surgery lasted two and a half hours.

On the 3rd postoperative day, patient complained of acute weakness of the right lower limb with tingling and numbness. Neurologic examination revealed her higher functions to be normal,no cranial nerve palsy, her upper limb sensory and motor functions were normal bilaterally. She had numbness over the anteromedial part of thigh and medial part of lower leg on both sides. Muscle testing was done for a) Hip flexion, extension, adduction and abduction, b) Knee flexion and extension and c) Foot dorsiflexion[3]. It revealed O/5 power in right lower limb. The knee and ankle jerks were absent in the right lower limb. Sensory examination revealed decreased sensitivity to light touch, pinprick, pain, and temperature over anteromedial part of thigh and medial portion of the right leg. Left lower limb examination was within normal limits.

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A definitive diagnosis could not be arrived at and MRI of lumbar spine and CSF examination was carried out. MRI revealed age related degenerative disc changes at L2 to L5 levels. Cerebrospinal fluid examination was within normal limit, and meningitis was ruled out. These finding were consistent with bilateral femoral neuropathy affecting more on right side. Nerve conduction studies were considered inconclusive at this stage and therefore, not performed.

Patient was reassured and managed with oral Multivitamin and Inj Dexamethasone 4mg thrice daily along with physiotherapy. Patient started improving and was discharged on the 15th postoperative day.She was followed up weekly; complete recovery was seen after 8 weeks. So the hypothetical diagnosis of bilateral femoral neuropathy was confirmed.

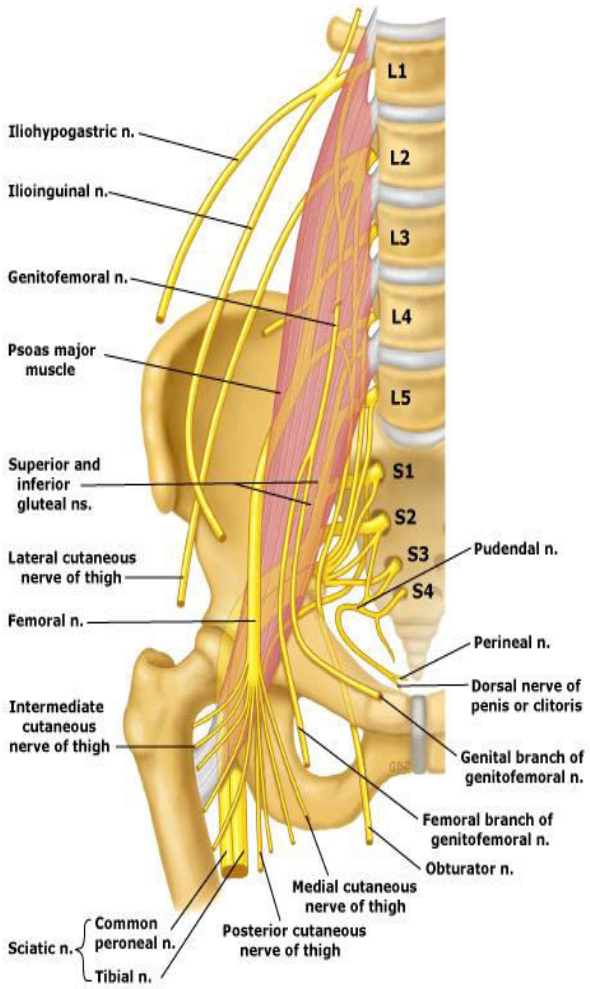

Fig.1 Anatomical relations of Femoral Nerve

Discussion:

Vaginal hysterectomy is performed in the lithotomy position and apart from the complications of regional anaesthesia, cases are reported in the literature that prolonged and improper lithotomy position results in complications like femoral neuropathy.

The femoral nerve is the largest branch of the lumbar plexus[4]. Muscles innervated by the femoral nerve are prime movers for leg extension at the knee joint, flexion at hip joint and critical for standing and stepping function.

The femoral nerve originates from the second, third, and fourth lumbar spinal nerves and innervates the anterior thigh muscles, hip and knee joints, and skin on the anteromedial thigh. Immediately after its formation the nerve penetrates the Psoas major muscle and continues downward within the substance of that muscle. It leaves it at the lower portion of its lateral border where it passes between the psoas and iliacus muscles. It exits from the abdominal cavity just below the inguinal ligament and lateral to the femoral artery. Below the ligament it divides into several branches to provide the motor supply to the quadricep muscles of the thigh, pectineus and sartorius muscles and occasionally to the long adductors[4].

Femoral nerve injury decreases sensation over the anterior and medial part of thigh and impairs the strength of quadriceps, hip flexion and patellar reflex. Proximal lesions at the level of the lumbosacral plexus may also decrease flexion of hip due to weakness of iliopsoas.

If the Femoral nerve is involved then the knee reflex may be decreased or absent, leading to a marked limp.

It is a general tendency to blame any neuropathy after subarachnoid block as being caused by the block. Hence, in the presence of any neurologic deficit, especially when an epidural or spinal anesthesia has been used, we should rule out the etiologies directly related to the neuraxial block, like spinal cord ischemia, direct trauma to a spinal nerve root or the spinal cord, chemical contamination of the local anesthetic solution, toxicity of the local anesthetic, or space-occupying lesion such as a hematoma or abscess. The causes which are not related to the neuraxial block include pre existing neurologic disease,neurologic injury due to malpositioning, and over stretching of the limbs during operative procedures. After proper history, the patient must be thoroughly examined and investigated to establish the exact cause of the neurologic deficit. A consultation with the neurologist is useful to confirm the correct diagnosis for medicolegal implications[5].

The intense analgesia and profound muscle

relaxation obtained by subarachnoid block make it possible to produce extremes of positioning. The single straight rod with swing stirrups helps to avoid sciatic and peroneal nerve palsies, but allows exaggerated abduction of the thighs with marked external rotation at the hip. This causes the femoral nerve to enter the thigh acutely angulated and twisted beneath the tough and inelastic inguinal ligament leading to compression of its vasa nervosa, thus producing local ischaemia of the nerve trunk. The duration for which this position is maintained is an important factor because, use of the same position for perineal operations lasting for less than one and a half hours is seldom associated with this neuropathy.This is in accordance with the case reported by Roblee[6].

One more factor which helps to increase the abduction of thigh and its external rotation, is that surgical assistants often lean against the inner aspect of the thighs.With the understanding of the pathogenesis,prevention becomes easy[4]. The excessive abduction of the thigh with rotation at hip needs to be prevented by lateral supports to the thigh. The reduced abduction of the thighs is inconvenient to the assisting surgeon, but this must yield to patient safety.

A lumbosacral spine magnetic resonance image was performed to rule out an epidural hematoma. Nerve conduction studies were considered inconclusive at this stage and were not available at our set up, therefore, not performed. Nerve conduction and electromyographic studies remain normal for 1 to 3 week after injury, and therefore, are not helpful in the initial diagnosis and therefore, should not be performed[7].

EMG can help to document the time and location of injury. After denervation, muscle fibers begin to discharge spontaneously, but changes are not seen until 2-3 weeks after injury. Thus, an abnormal EMG obtained within the first week following a regional anesthetic is useful for determining pre existing disease. Injury at the level of the nerve root should affect both the anterior and the posterior rami. If the paraspinous area (supplied by the posterior ramus) is not affected, then the level of nerve injury is distal to the nerve root and not caused by central neuraxial anesthesia[9].

In the present case, in the lithotomy position with swing stirrups, for more than two and a half hours could have resulted in femoral nerve ischaemia causing neuropathy of femoral nerve. This is the most unphysiological position resulted in the exaggerated abduction and external rotation at the hip, leading to kinking and twisting of the femoral nerve beneath the tough inguinal ligament and thus producing ischaemia of the nerve trunk resulting in the loss of function.The recovery and the overall prognosis is excellent in these cases.The recovery is spontaneous and starts within three to four weeks and gets completed in six to eight weeks. The present case started recovering and was able to walk after 8 weeks..

To prevent femoral nerve injury during vaginal hysterectomy, one should avoid extremes of hip flexion abduction, and external rotation in the lithotomy position. Roblee[6] constructed lateral thigh supports to limit excessive abduction and external rotation of the hips. These supports have been used in 34 patients in the lithotomy position and have been found to be comfortable. During the operation, surgeons should avoid leaning against the patient's thighs.Based on the few previous reports, femoral neuropathy after vaginal hysterectomy usually occurs when the patient is in the lithotomy position with swing stirrups for more than two & a half hours[9,10]. Other preventive measures include: minimizing operative time; if it is longer than one & a half hours, change the patient's posture to relieve the pressure on the femoral nerves. Palpate the femoral artery below the inguinal ligament before, during, and after the operation. If the femoral pulse is diminished, it is necessary to adjust the patient's posture. Check possible risk factors (eg, diabetes mellitus, low BMI, etc) that might cause femoral neuropathy and offer preventive measures.

Conclusion:

Proper patient positioning focusing on pressure management requires not only a knowledge of anatomy and physiology but also familiarity with appropriate positioning devices and solid teamwork. Every member of the team must continually assess the patient throughout the procedure to ensure that appropriate positioning is a focal point of patient care. Positioning must be carefully planned and executed to minimize risks and maintain optimal patient safety.

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Case Report

Long Term Follow up of a Tripod Design Anterior Chamber Intraocular Lens (ACIOL)

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Abstract:

A 45 year old male presented with partially exposed haptic loop of a tripod design anterior chamber intraocular lens (ACIOL) in the right eye. The best corrected vision was 20/60 right eye and 20/20 left eye. The patient refused surgical intervention of the right eye ACIOL in view of good vision. The patient was counselled against high risk of endophthalmitis and kept under close observation since last few years. We report a case of exposed loop of ACIOL since last 5 years with no complications.

Key Words: Exposed Haptic, Anterior Chamber IOL, Explantation of IOL

Introduction:

Intraocular lens implantation (IOL) was first done by Sir Harold Ridley in 1949 at Thomas Hospital London [1]. Complications of anterior chamber IOL are extrusion, dislocation, decentration, endothelial decomposition, inflammation and glaucoma [2, 3, 4]. Dislocation of intraocular lens outside the eye is one of the indications of explanting the IOL [5]. The most common complication which may be associated with exposed haptic is endophthalmitis.[2-6] We report a case of exposed haptic loop of ACIOL due to chronic rubbing following post traumatic cataract surgery.

Case Report:

A 45 years old male patient underwent right eye cataract surgery for post traumatic cataract 13 years back. A tripod design anterior chamber intraocular lens (ACIOL) was implanted in the right eye. The best corrected visual acuity (BCVA) was documented as 20/60 right eye and left eye was asymptomatic with BCVA 20/20.

The patient was a known case of allergic conjunctivitis for which he received symptomatic treatment over the last 15-20 years. The patient presented 5 years back with complains of foreign body sensation in right eye.

On examination one of the haptic of the tripod ACIOL was exposed and loop of the haptic was external to the eye (Fig. I & II). However, the patient maintained BCVA of 20/60 right eye. There was no anterior chamber reaction and no evidence of infection. The intraocular pressure was 12mm of Hg right eye and 14 mm Hg left eye. The specular count of the right eye was 840 cells/mm^2.

In view of high risk of endophthalmitis, the patient was counselled for explantation of ACIOL under explained risk of endothelial failure. However, the patient refused IOL explanation in view of relatively good vision and lack of symptoms. The patient was asked to remain under close follow up due to risk of infection. Over the follow up of last 5 years, there has been no episode of infection or reaction. The patient is asymptomatic maintaining BCVA of 20/60 right eye. The specular count has decreased to710 cells/mm^2, while intraocular pressure is normal.

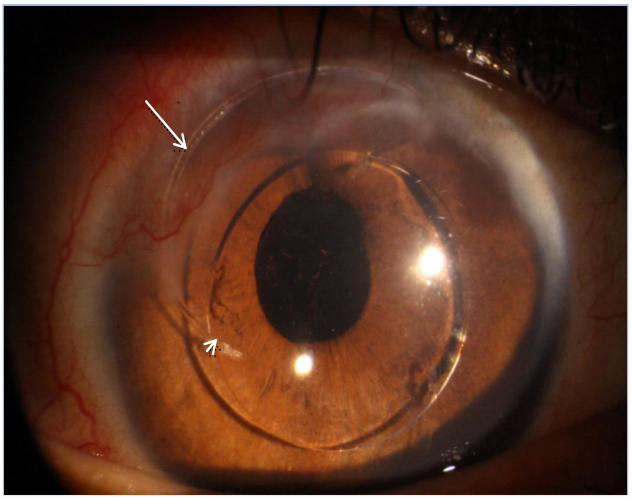

Fig. I: Exposed Haptic of tripod ACIOL (arrow showing exposed part of ACIOL haptic & arrow head showing intra occular part of haptic).

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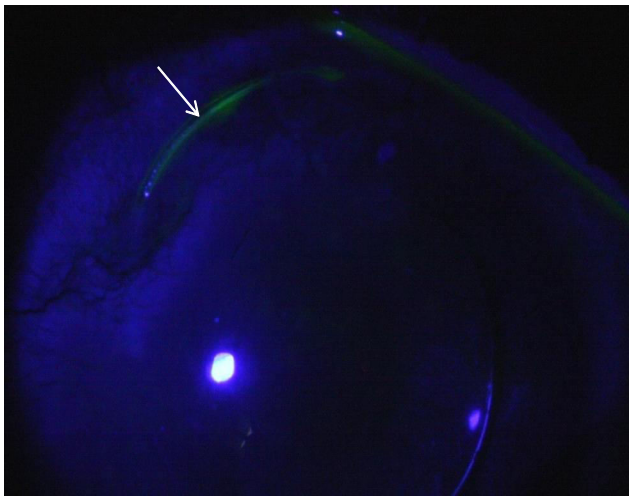

Fig. II: Fluorescein staining showing exposed part of the haptic.

Discussion:

Exposure of haptic of anterior chamber has been reported in the past due to trauma, eye rubbing or due to infections.[6] In our case the patient was a known case of allergic conjunctivitis and eye rubbing may have been the cause of limbal thinning and haptic extrusion. There was no leak of aqueous from anterior chamber and pressure Siedel test was negative at all examinations.

Risk of endophthalmitis is high following such exposed haptic and it is advisable to explant the IOL or exchange it.[7-11] However due to critically low endothelial count, risk of endothelial decompensation is also high. Our patient refused surgical intervention because he was asymptomatic and maintained good vision.

On regular follow up no fresh complains were noted. Possible reasons for prevention of endophthalmitis could be that the exposed haptic was covered with upper lid and not exposed to the environment. Also there was no leakage of aqueous and anterior chamber depth was maintained. The chronic trauma due to rubbing and subsequent surrounding inflammation and fibrosis must have sealed any leakage areas around the haptic loop. To the best of our knowledge this is the first case of an exposed IOL haptic which has remained asymptomatic on regular follow up for last 5 years.

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Review Article

Biology of Receptor Activator of Nuclear Factor Kappa-B Ligand (RANKL) and Osteoprotegerin (OPG) in Periodontal Health and Disease - A Review

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Abstract:

Periodontitis is a destructive disease that targets tooth-supporting structures through complex and multifactorial pathogenic processes. Alveolar bone destruction, a hallmark of periodontitis progression and one of the major causes of tooth loss in human, is mediated by the host immune and inflammatory response to microbial challenge. The discovery of the receptor activator of nuclear factor-kappa B (RANK)/ RANK ligand (RANKL)/osteoprotegerin (OPG) axis has improved the knowledge of bone metabolism regulation. The RANKL/RANK interaction is needed for differentiation and maturation of osteoclast precursor cells to activate osteoclasts and for the survival of mature osteoclasts. Osteoprotegerin is the naturally occurring inhibitor of osteoclast differentiation. It binds to RANKL with high affinity and blocks RANKL from interacting with RANK. The RANKL/OPG ratio is increased in periodontitis compared to healthy individuals, suggesting that this molecular interaction may be important in modulating local bone loss.

In recent decades, studies on cellular and molecular mechanisms of bone loss in periodontitis have suggested that the use of host modulation agents is an important adjunctive therapy to scaling and root planning. This line of investigation is expected to help in the development of new therapeutic approaches to stop progressive bone resorption induced by oral bacterial challenge.

Key Words: Bone resorption, osteoprotegerin; periodontitis; RANKL.

Introduction:

The bone is an engineering feat; it is strong but light enough to permit locomotion, rigid to allow muscles to be fixed but capable of bending without breaking and its structure is programmed for variable loading. In addition to its structural role, bones also serve as a reservoir for calcium. This means that bone is malleable and its structure can be sampled, adapted or fine tuned for the process of remodeling.

As per glossary of periodontal terms (2001), periodontitis is defined as inflammation of the supporting tissues of the teeth. Usually a progressively destructive change leads to loss of bone and periodontal ligament. Balance between bone resorption by osteoclasts and bone formation by osteoblasts determines the level of bone mass. The remodeling of bone takes place in so called "bone multi-cellular units" (BMU's) and is initiated by recruitment, formation and activation of bone resorbing osteoclasts. They are activated by RANKL and by integrin-mediated signalling from bone matrix itself [1].

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Osteoclast differentiation is regulated by osteoblasts. Receptor activator of nuclear factor kappa B ligand and its decoy receptor, osteoprotegerin, are essential molecules for osteoclast differentiation supported by osteoblasts.

Our understanding of the molecular mechanisms that regulate osteoclasts formation and activation has advanced rapidly during the past decade since the discovery of RANKL/RANK signaling system and following the development in the late 1980's of *in vitro* assays that facilitated harvesting of large numbers of osteoclasts precursors (OCP's) from the bone marrow or spleen, which could then be cultured in the absence of osteoblasts/stromal cells. An early indication that RANKL and OPG could be of relevance to the periodontium came from *in vitro* work demonstrating that periodontal ligament cells do produce RANKL and OPG and they can as well support osteoclastogenesis through RANKL signalling[2]. Both osteoblasts and periodontal ligament fibroblasts are stimulated with lipopolysaccharide and IL-1 express RANKL, suggesting that once the inflammation extends into the periodontal ligaments and alveolar bone, alveolar bone resorption might be accelerated through the increased expression of RANKL. The periodontopathic bacteria *A. actinomycetemcomitans*

and *P. gingivalis* have unique mechanisms to induce RANKL in osteoblasts and gingival fibroblasts. Receptor activator of nuclear factor-kappa B ligand and OPG expression might also be related to the function of amelogenin, and regulation of odontoclast formation[3]. An appreciation of the relationship between immune processes and the bone metabolism in various inflammatory bone diseases has given rise to the field of osteoimmunology[4].

This field has given a future outlook to study the basis of periodontal destruction. Hence, further research is required on osteoimmunology which will make the molecular mechanisms of bone destruction clear and a novel diagnostic parameter and therapies in periodontics can be devised.

Regulation of Oteoclast Formation and Activation:

Osteoclasts are multinucleated bone resorbing cells formed by cytoplasmic fusion of their mononuclear precursors, which are in the myeloid lineage of hematopoietic cells that also give rise to macrophages. The switch to osteoclasts differentiation requires expression of c-Fos (proto-oncogene) by the osteoclast precursors cells[5]. To resorb bone effectively, osteoclasts attach themselves firmly to the bone surface using specialized actin – rich podosomes, which they use to form tightly sealed circular extension of their cytoplasm with the underlying bone matrix. Within these sealed zones they form ruffled membranes that increase the surface area of the cell membrane for secretion of hydrochloric acid and the proteolytic enzyme cathepsin K. There they simultaneously destroy the inorganic and organic matter of bone, while protecting neighboring cells by this sealing mechanism. They are activated by RANKL and integrin mediated signaling pathway from the bone matrix[1]. Osteoclasts are required during embryonic development for the removal of bone trabaculae formed under growth plates during endochondral ossification and thus for formation of the bone marrow cavity to facilitate normal hematopoiesis. Failure of osteoclast formation or activity results in osteoporosis, some forms of which are lethal because of attendant immunodeficiency and increased risk of fractures.

Osteoclasts work in packs within remodeling units under the of osteoblast lineage cells expressing macrophage colony stimulating factor (M-CSF) and RANKL. The strategy for acquiring OCP's from sources was developed in the knowledge that M-CSF expression by osteoblast/stromal cells was required for progenitor cells to differentiate into osteoclasts, but that M-CSF on its own was unable to complete this process. This requirement for M-CSF was based on the observation that op/op mice, which do not express functional M-CSF, have osteopetrosis because of a lack of osteoclasts. Rodan & Martin[6] proposed the novel hypothesis that osteoblast/stromal cells play a central role in the regulation of osteoclast formation and bone resorption. Many investigators had attempted to identify the osteoclast-activating factor that completed the differentiation of precursors that had been exposed to M-CSF.

Rankl:

Receptor activator of nuclear factor kappa-B ligand is known as tumor necrosis factor ligand superfamily member 11(TNFSF11), TNF-related activation-induced cytokine(TRANCE), osteoprotegerin ligand (OPGL) and also as osteoclast differentiation factor (ODF). Receptor activator of nuclear factor kappa-B ligand is a type II homotrimeric transmembrane protein that is expressed as a membrane- bound and a secreted protein, which is derived from the membrane form as a result of either proteolytic cleavage or alternative splicing[7]. Three human RANKL isoforms - hRANKL1, hRANKL2 and hRANKL3 are identified. hRANKL1 possesses intracellular, transmembrane and extracellular domains. Intracellular domains are abesnt in hRANKL2 and hRANKL3. hRANKL3 additionaly does not possess transmembrane domains 8 . The proteolytic cleavage of RANKL requires ADAM (a disintegrin and metalloprotease domain) and matrix metalloproteases[9]. Receptor activator of nuclear factor kappa-B ligand expression is stimulated in osteoblast/stromal cells by most of the factors that are known to stimulate osteoclast formation and activity. It is highly expressed in lymph nodes, thymus and lung, and at low levels in a variety of other tissues including spleen and bone marrow[10]. In inflamed joints it is expressed by synovial cells and secreted by activated T cells. These sources of RANKL appear to be responsible, at least in part, for mediating the joint destruction in patients with rheumatoid arthritis[11]. Tumor Necrosis Factor also mediates joint destruction in rheumatoid arthritis by systemically increasing the number of circulating OCPs, and by promoting their egress from the bone marrow into the peripheral blood and then to the inflamed joints, where it promotes fusion of these cells to osteoclasts along with RANKL and interleukin-l[12].

Receptor activator of nuclear factor kappa-B ligand like TNF, stimulates the release of immature progenitors into the circulation. However, RANKL does not induce OCP mobilization in protein tyrosine phosphatase-c deficient mice. Thus making osteoclasts defective in terms of bone adhesion and resorption[13]. Thus, RANKL induced osteoclast activation may regulate progenitor recruitment as part of homeostasis and host defense, linking bone remodeling with regulation of hematopoiesis. Preclinical studies in mice have shown that RANKL is also expressed in mammary epithelial cells during pregnancy and is required for lactational hyperplasia of mammary epithelial cells and milk production[14]. It is also expressed by some malignant tumor cells that also express RANK, and thus it may play a role in inducing tumor cell proliferation by an autocrine mechanism or in a paracrine manner if it is produced by accessory cells, such as activated T cells[15]. However, production by T cells of RANKL also induces expression of interferon-13 by activated osteoclasts through c-Fos to negatively regulate their formation[16]. This mechanism can be enhanced by T-cell produced interferon-y, which degrades TNF receptor associated factor (TRAF), an essential adapter protein that is recruited to RANK to mediate RANK signaling [17].

Rank:

Receptor activator of nuclear factor kappa-B is a type I homotrimeric transmembrane protein whose expression was initially detected only on OCPs, mature osteoclasts, and dendritic cells. Like RANKL, however, it is expressed widely. Receptor activator of nuclear factor kappa-B ligand protein expression has been reported in mammary gland and some cancer cells, including breast and prostate cancers, two types of tumors with high bone metastasis potential. Although no human have been identified to date with inactivating mutations or deletions of RANK, a deletion mutation occurred spontaneously in a line of transgenic mice, which consequently had all of the features of mice with targeted deletion of RANK, confirming the importance of RANK for osteoclast formation[18]. Activating mutations in exon 1of RANK causes an increase in RANK-mediated nuclear factor-kappa B (NF kappa-B) signaling and a resultant increase in osteoclast formation and activity, account for the increased osteolysis seen in some patients with familial Paget's disease and have confirmed the importance of this system in humans[19].

Osteoprotegerin:

Osteoprotegerin also known as osteoclastogene -sis inhibitory factor (OCIF) is a basic glycoprotein which acts as a decoy receptor of RANKL. It is expressed in many tissues apart from osteoblasts, including heart, kidney, liver, spleen and bone marrow. Its expression is regulated by most of the factors that induce RANKL expression by osteoblasts. Although there are contradictory data, in general up regulation of RANKL is associated with down regulation of OPG, or at least lower induction of OPG, such that the ratio of RANKL to OPG changes in favor of osteoclastogenesis. Many reports have supported the assertion that the RANKL/OPG ratio is a major determinant of bone mass[20]. An osteoprotective role for OPG in humans is supported by the report of homozygous deletions of 100 kilo bases of OPG in two patients with juvenile Paget's disease, an autosomal-recessive disorder chazacterized by increased bone remodeling, osteopenia and fractures[21]. It is also supported by the identification of an inactivating deletion in exon 3 of OPG in three siblings with idiopathic hyperphosphatasia, which is an autosomal-recessive bone disease characterized by increased bone turnover associated with deformities of long bones, kyphosis, and acetabular protrusion in affected children[22]. A recent surprising finding is that OPG expression is regulated by Wnt/â-catenin signaling in osteoblasts, the same pathway that regulates osteoblastic bone formation[23]. Thus, bone mass is determined by the combined efforts of osteoblasts and osteoclasts, and is regulated in osteoblasts by two major signaling pathways: RANKL/RANK and Wnt/â-catenin. OPG also appears to protect large blood vessels from medial calcification, based on the observation of renal and aortic calcification occurring in OPG knockout mice[24]. Furthermore, the absence of OPG in OPG/ apolipoprotein E double knockout mice accelerates the calcific atherosclerosis that develops in apolipoprotein E knockout mice, suggesting that OPG protects against this complication of atherosclerosis[25]. Whether OPG and RANKL signaling plays important roles in cardiovascular disease remain to be determined and is controversia1. For example, there is also an association between high levels of OPG in serum and cardiovascular disease, diabetes, and chronic renal failure in humans[26]. However, OPG in this latter setting does not appear to protect the skeleton against the increased bone resorption of secondary hyperparathyroidism mediated by PTH in patients with renal osteodystrophy or against vascular calcification. It is possible that OPG in the serum of such patients is bound to a plasma protein(s) and thus

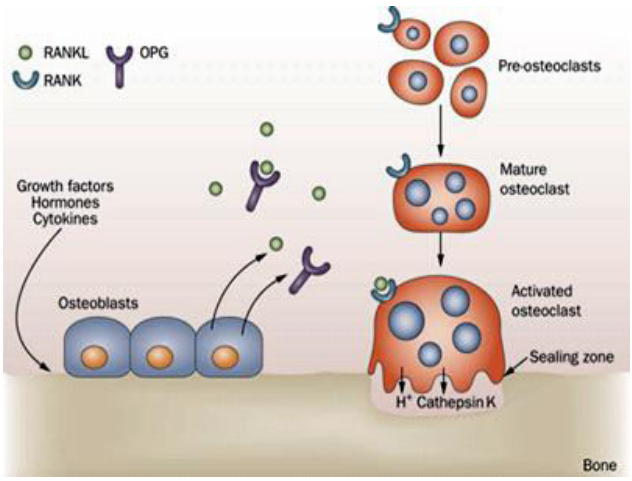

Fig. I: RANKL-RANK-OPG interplay

rendered inactive, but further studies will be required to determine the significance of these observations, which question whether the RANKL/OPG ratio in serum is indicative of bone mass/bone resorption in these settings[27].

Possible Therapeutic Approaches for Inhibition of Periodontal Bone Loss by Targeting Rankl:

We know that the production of RANKL from bacterial antigen-specific T and B cells seems to trigger periodontal bone loss and that the suppression of antigen-specific T and B cell responses may sufficiently facilitate down-modulation of periodontal bone destruction. Thus, we might envision an ideal therapy that suppresses the bone destructive consequences of antigen-specific T and B cells while, at the same time, permitting the homeostatic bone remodeling mediated by RANKL-produced from osteoblasts and bone marrow stromal cells. Indeed, interference with co-stimulatory molecules, which are required for induction of antigen-specific T and B cells, abrogated periodontal bone resorption. In other words, systemic administration of CTLA4Ig, a functional antagonist of CD28 binding to B7[28] or anti-CD40 ligand antibody to inhibit CD40/CD40L[29], could theoretically abrogate bone resorption in an animal periodontal model. In addition to these approaches, we are now challenged to establish new therapeutic regimens to mediate the antigen-specific T and B cells. For example, one approach that is attracting wide attention involves the utilization of regulatory CD4+ T cells, which play a suppressive role in inflammation caused by the activation of adaptive T cell responses[30]. Accordingly, the therapeutic application of T cells to modulate periodontal bone loss can be researched. This line of investigation is expected to help in the development of new therapeutic approaches to stop progressive bone resorption induced by oral bacterial challenge.

Discussion

As compared to healthy gingival tissues, periodontitis affected tissues had higher RANKL and lower OPG molecules[31]. Studies on RANKL/OPG ratio, demonstrated 2.2-fold increase in chronic periodontitis when compared to healthy individuals[32] or equally elevated levels in chronic and aggressive periodontitis, compared to individuals who were healthy or had gingivitis[33]. Other studies also demonstrate the correlation between RANKL/OPG ratio in GCF and gingival inflammation, which indicates that this ratio has specificity to determine periodontal bone destruction[34]. With regards to microbiota the presence of *P.gingivalis* in subgingival biofilms at chronic periodontitis sites, positively correlated with RANKL tissue gene expression levels or the RANKL/OPG ratio but not with OPG[32]. Similarly a positive correlation was found between RANKL total amounts in GCF and the subgingival presence of *P. gingivalis* and *T.denticola* in chronic periodontitis but no correlations were found in healthy individuals[35]. Hence, these studies warrant that if OPG is increased or RANKL inhibited, it will have a positive effect on the periodontium. Thus this approach was used in an experimental study, where concomitant administration of OPG in T-cell specific A. actinomycetemcomitans induced periodontitis model in mice, diminished alveolar bone destruction and reduced osteoclast numbers[36]. In another periodontitis model, effects of an anti-RANKL antibody on periodontal bone resorption were tested. Results showed that antibody to RANKL can inhibit A. actinomycetemcomitans-specific T cell-induced periodontal bone resorption by blockade and reduction of tissue RANKL, providing an immunological approach to ameliorate immune cell-mediated periodontal bone resorption[37]. Thus it can be implied that inhibition of RANKL by OPG or direct can have a beneficial effect on the outcome of periodontal disease treatment and also prevent its recurrence and prevent further alveolar bone resorption.

Conclusion:

From this review it can be concluded that RANKL-OPG axis is one of the most important factor to determine the ongoing periodontal disease activity.

The RANKL–RANK–OPG axis is clearly involved in the regulation of bone metabolism in periodontitis, in which an increase in relative expression of RANKL or a decrease in OPG can tip the balance in favor of osteoclastogenesis and the resorption of alveolar bone. Post treatment high RANKL/OPG ratio indicates that the molecular mechanisms of bone resorption are still active, and the affected periodontal sites are at a potential risk for developing the disease again. Hence additional therapies to modulate the immune system which will target the RANKL-OPG axis to provoke a host response which will be beneficial in the long term periodontal management. Hence in addition to the long term clinical and prospective studies more studies are required, which will monitor the periodontal disease progression and the progressive changes in the RANKL-OPG level before and after treatment and during the maintenance phase also. In addition it can be concluded that any kind of interference with the RANKL–RANK–OPG axis may have a protective effect on periodontal bone loss. Such interference may form the basis for rational drug therapy in periodontics in the future.

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